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Pesticide Assessment Guidelines
Subdivision D: Product Chemistry

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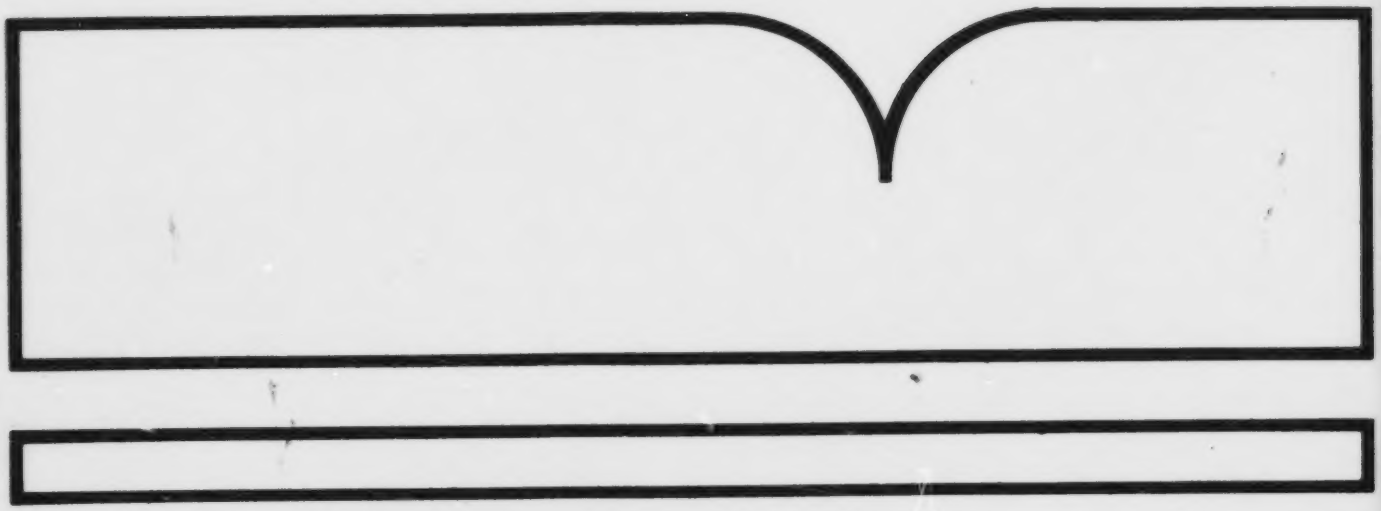

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SUBDIVISION D

PRODUCT CHEMISTRY

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16. Abstract (Limit: 200 words)

Subdivision D, a Federal Insecticide Fungicide and Rodenticide Act guideline, was the the subject of close final review from an Agency-sponsored comittee consisting of a representatives from industry, academia and a national environmental group.

To assess its potential toxicity to humans and hazard to the environment, the Agency requires basic information on the composition of each product. For all products this information includes a description of the manufacturing process, a discussion on the formation of product impurities and a Confidential Statement of Formula. This statement names each intentional ingredient (both active and inert) of the product, impurities ($\geq$ 0.1%) that are associated with the active ingredient, and any other product impurities that may be either toxicologically significant or environmentally hazardous. The formulating composition (i.e., nominal concentration in percentage by weight) is indicated and composition limits, upper and lower, are stated for the intentionally added ingredients; upper limits, for each impurity. For products produced by an integrated-formulation system, composition data determined by an analysis are needed for the product and in some instances for the technical chemical.

Subdivision D constitutes one volume of a twelve-part NTIS Federal Insecticide, Fungicide and Rodenticide Act guideline series.

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FOREWORD

Subdivision D describes protocols which may be used to perform Product Chemistry testing to support the registration of pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). It is a nonregulatory companion to 40 CFR Part 158, Data Requirements for Registration. A public meeting was held in July, 1982 to accept comments on the FIFRA guidelines. Because of the importance of the issues raised in the Subdivision D comments, a review committee comprised of representatives of industry, environmental groups and academia read and approved the Agency revision. This guideline refers to requirements established in 40 CFR Part 158 so that this document can be read as a complete package and so that the protocols may be explained in their proper context.

SUBDIVISION D: PRODUCT CHEMISTRY

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I. BACKGROUND AND SCOPE

A. History.

1. Product Chemistry guidelines. Guidelines proposing data requirements for product chemistry information were first proposed by the Agency on June 25, 1975 in 40 FR 26802. The guidelines published at that time also included data requirements for other types of studies, such as studies to evaluate environmental chemistry (fate), fish and wildlife hazard, human hazard, and product performance. These proposed guidelines described the kinds of information required by the Agency to determine whether a particular pesticide should be registered.

The interested public submitted more than 80 sets of comments on the 1975 proposed guidelines. Based on a review of these comments and extensive Agency consideration, EPA reproposed the product chemistry guidelines as part of Subpart D of Part 163 in Title 40 of the Code of Federal Regulations (43 FR 29696, July 10, 1978). At the same time, EPA also reproposed the Introduction (Subpart B), Environmental Chemistry guidelines (then also part of Subpart D), and the guidelines for hazard evaluation to protect wildlife and aquatic organisms (Subpart E).

In response to the 1978 proposals ("1978 proposed guidelines"), the Agency again received over 80 sets of comments. The Agency has considered these comments in developing the final Product Chemistry guidelines. In general, EPA has revised Subdivision D to clarify the guidelines, to enhance the quality of the data that would be submitted, and to reduce the burden on applicants or registrants (to the extent that this could be done while still assuring that EPA obtained the needed information).

2. Change from the 0.01 Percent Requirement to a 0.1 Percent Requirement. The 1978 proposed guidelines proposed the identification and quantification of each substance in the pesticide product, including added ingredients and/or impurities, greater than or equal to 0.01 percent of the product by weight. The Agency received many public comments objecting to this requirement. Forty-four percent of the comments received on the product chemistry guidelines opposed the Agency's proposed requirement for quantitative data on product ingredients (inerts and impurities) equal to or greater than 0.01 percent by weight. The commenters also said that the quality control procedures associated with maintaining the certified composition limits for all of the product ingredients would be excessive. Actually, however, the 0.01 percent requirement was placed only on manufacturing-use products and products produced by an integrated formulation system; the requirement for other formulated products was less demanding.

Most of the commenters also said that the costs of certifying product composition to the proposed 0.01 percent level would be extremely high, amounting to more than 10 percent of the total development costs of a typical pesticide. The estimates varied widely and were dependent upon cost estimates for developing methodology to detect each impurity ($7,000 to $25,000) and the number of product impurities.

Companies formulating with polymeric materials, or with oils containing perhaps hundreds of minor components, pointed out the problem of analytical closure (viz., the determined ingredients do not add to 100 percent, often with a difference of a few percentage points) and considered it virtually impossible to account for all components present in quantities greater than or equal to 0.01 percent by weight. They also stressed that previously the Agency had frequently been concerned with product impurities of toxicological significance at levels considerably less than 0.01 percent, and they urged the Agency to limit the 0.01 percent requirement to only those impurities.

Although supporting the Agency's concern about trace quantities of highly toxic impurities, several of these commenters proposed, as an alternative approach, the development of quantitative methodology for only those impurities having sufficient toxic activity to be potentially hazardous to man and the environment. Many such comments were offered in conjunction with the proposed requirements for certification of limits. Three examples of these many comments follow:

> (1) A more reasonable requirement would be to request applicants to advise the Agency on biologically active ingredients that could likely be present in the product at levels that could affect product safety.
>
> (2) The certification of limits, therefore, must be selectively aimed at and limited to the active ingredient content and those impurities known to represent a toxicological hazard at the levels found.
>
> (3) These limits should be set only for the active ingredient and potentially highly toxic impurities.

The Agency is in agreement with the ideas set forth by these commenters but has decided not to ask for biological-screening data at this time because of the many subsantial issues raised to these tests by the public. Instead, the Agency will rely upon the information and data submitted under other guideline sections (i.e., Manufacturing process, Discussion of the formation of impurities, Preliminary analysis of products) to provide adequate data on product composition. Based on a review of this data, applicants would be required to provide analytical methodology suitable for monitoring the commercial product both for the active ingredients and for impurities that are of toxicological concern or environmentally hazardous.

Table 1. Organization of product chemistry topics in current guidelines and 1978 proposed guidelines.

Subject	DESIGNATED AND REDESIGNATED SECTIONS Guideline Sections and Paragraphs Current	 Proposed in July 1978
GENERAL INFORMATION		
Scope of data requirements	60-1(a)	163.60-1(a)
List (or location) of requirements	-1(c)	-2(a)
DEFINITIONS	60-2(a) thru (m)	163.61-1(a) thru (c 163.40-2(a),(c),(d)
GENERAL PROVISIONS (requirements)		
Data on pesticide product	60-3(a)	.....
Requests for waivers	-3(b)	.....
Explanations for excluding data	.....	163.61-2(e)
Tech. grade of the active ingredient	.....	-2(b)
Timing of data submission	-3(c)	.....
Data for products not in production	-3(c)(1)	-2(c)
Contents of deferral request	-3(c)(2)	.....
Notification requiring deferred submittal	-3(c)(3)	.....
Nature of data submittals	.....	-2(d)
Confidential treatment of data	-3(e)	.....
PRODUCT IDENTITY AND DISCLOSURE OF INGREDIENTS		
Product identity	61-1(a)	163.61-3(a)
Formula of technical chemical	.....	-3(b)
Statement of formula	-1(b)	-3(c)
Name and certified limits for added ingredients	-1(b)(1)	.....
Name and certified limits for impurities	-1(b)(2)	.....
Purpose	-1(b)(3)	.....
Chemical name and CAS-Registry number	-1(b)(4)	-3(c)(1)
Other names, formulae, molecular Wt., etc.	-1(b)(5)	-3(c)(2)-(6)
DESCRIPTION OF BEGINNING MATERIALS AND MANUFACTURING PROCESS		
Beginning materials	61-2(a)	163.61-4(a)
Submittal of registration number of manufacturing-use product	-2(a)(1)	.....
Name and address of producer	-2(a)(2)(i)	.....
Names of beginning materials	-2(a)(2)(ii)	-3(a)
Specifications, etc.	-2(a)(2)(iii)	.....
All other information	-2(a)(2)(iv)	.....
Manufacturing process	-2(b)	-4(b)
Batch or continuous	-2(b)(1)	-4(b)
Amounts and order of addition	-2(b)(2)	-4(b)
Equipment	-2(b)(3)	-4(b)

Table 1 (continued)

Physical conditions	-2(b)(4)	-4(b)
Reactions	-2(b)(5)	-4(b)
Flow chart	-2(b)(6)	-4(b)
Duration of steps	-2(b)(7)	.....
Purification	-2(b)(8)	-4(b)
Quality control	-2(b)(9)	-4(b)
Changes	-2(c)	.....
DISCUSSION ON FORMATION OF IMPURITIES		
General requirements	61-3(a)	163.61-5
Manufacturing-use products and end-use products from integrated formulation system	-3(b)	.....
Impurities greater than 0.1% (expected)	-3(b)(1)	.....
Other impurities (found)	-3(b)(2)	.....
All other end-use products	-3(c)	.....
ANALYSIS OF PRODUCT SAMPLES		
When required	62-1(a)	.....
Requirements	-1(b)	163.61-7(a)(1)
Selection of samples	-1(b)(1)	-7(b)(1)
Number of samples	-1(b)(1)(i)	-7(b)(1)
Batch choice	-1(b)(1)(ii)	-7(b)(1)
Intervals choice	-1(b)(1)(iii)	-7(b)(1)
Additional samples	-1(b)(1)(iv)	.....
Ingredients to look for	-1(b)(2)	.....
Selection of method	-1(b)(3)	-7(a)(1)
Additional requirements	-1(b)(4)	-7(a)(5)
Methods and reporting of results	-1(c)	-7(a) & (b)
Methods description	-1(c)(1)	-7(a)(1)
Precision and accuracy of method	-1(c)(1)(ii)	-7(a)(1)
Reporting results	-1(c)(2)	-7(b)
Identifying spectral data	-1(d)	-7(b)(2)
CERTIFICATION OF INGREDIENT LIMITS		
General information	62-2(a)	.....
Requirements and considerations	-2(a)(1)	163.61-6(b)(1)
Submittal of explanations	-2(a)(2)	163.61-6(b)(2)
Expression of limits	-2(a)(3)	-6(a)
Acceptable ranges of limits	-2(a)(4)	.....
Duration of limits	-2(a)(5)	-6(b)(4)
Enforcement of limits	-2(a)(6)	.....
Revision of limits	-2(a)(7)	-6(b)(3)
Manufacturing-use products and end-use products from integrated formulation system	-2(b)	.....
All other end-use products	-2(c)	.....
Additional ingredient, impurities	-2(d)	.....

Table 1 (continued)

ANALYTICAL METHODS TO VERIFY CERTIFIED LIMITS		
When required	62-3(a)	.....
Requirement for analytical methods	-3(b)	163.61-7(a)(1)
Substances requiring methods	-3(b)(1)	-7(a)(2)-(4)
Manufacturing-use products and end-use products from integrated formulation system	-3(b)(1)(i)	-7(a)(2),(3)
All other end-use products	-3(b)(1)(ii)	-7(a)(4)
Additional ingredients	-3(b)(1)(iii)	-7(a)(5)
Waivers	-3(b)(2)	.....
Precision and accuracy of methods	-3(b)(3)	-7(a)(1)
Validation studies	-3(b)(4)	-7(a)(1)
Method description and reporting	-3(c)	-7(a)(1)
PHYSICAL AND CHEMICAL CHARACTERISTICS		
General provisions	63-1	163.61-8(a),(b),(c)
Color	-2	-8(c)(1)
Physical state	-3	-8(c)(7)
Odor	-4	-8(c)(2)
Melting point	-5	-8(c)(3)
Boiling point	-6	-8(c)(9)
Density, bulk density, or specific gravity	-7	-8(c)(8)
Solubility	-8	-8(c)(4)
Vapor pressure	-9	-8(c)(10)
Dissociation constant	-10	-8(d)
Octanol/water partition coefficient	-11	-8(c)(6)
pH	-12	-8(c)(11)
Stability	-13	-8(c)(5)
Oxidizing or reducing action	-14	-8'c)(12)
Flammability	-15	-8(c)(13)
Explodability	-16	-8(c)(15)
Storage stability	-17	-8(c)(13)
Viscosity	-18	-8(c)(17)
Miscibility	-19	-8(c)(16)
Corrosion characteristics	-20	-8(c)(18)
Dielectric breakdown voltage	-21	-8(c)(19)
SUBMITTAL OF SAMPLES	64-1	163.61-9

B. Reorganization of Guidelines Sections.

In order to present the revised Product Chemistry guidelines in a more logical sequence, the Agency has rearranged and renumbered the sections and their individual requirements. Table 1 indicates the sections and principal paragraphs of the current guidelines and their designations in guidelines proposed in 1978.

C. Purposes of Product Chemistry Data Guidelines.

The Agency intends that the guidelines provide meaningful information to applicants, registrants, and the general public regarding the product chemistry data requirements for registration of a pesticide. Such guidance should enable the members of the pesticide industry to plan their research programs using test methods acceptable to the Agency, and to anticipate the costs as well as the time involved in preparation and approval of an application for registration. Toward these ends, these guidelines specify: the conditions under which each data requirement is applicable; the standards for acceptable testing, stated with as much specificity as the current scientific disciplines can provide; and the information required in a test report. The guidelines also suggest circumstances under which an applicant should consult with the Agency before initiating a test. In addition, the guidelines provide examples of acceptable protocols for conducting the required testing, and cite - in sections on specific tests - published literature which provides information useful for designing tests.

The Agency believes that adherence to this subdivision will result in reliable data to support applications for registration, and will accelerate and upgrade the Agency's review and evaluation of registration applications.

Data submitted to meet the requirements for Product Chemistry of this subdivision fall into two major categories: information on product composition and information on specific chemical and physical characteristics of pesticide chemicals and products.

1. Product composition. Data on product composition include information about the beginning materials and manufacturing process (§ 61-2), the discussion on formation of impurities (§ 61-3), the results of preliminary analysis of product samples (§ 62-1), the explanation of how the certified limits were determined (§ 62-2), and the description of and validation data for analytical methods for ingredients (§ 62-3). These data support the conclusions expressed in the statement of formula required by § 61-1.

Product composition data are used in several ways. First, EPA reviews the composition of a product to determine whether the product contains any ingredient in an amount which may cause unreasonable adverse effects on the environment. This review is based on information available to EPA from the public literature and its own files about the toxicity and environmental effects of ingredients. This is the primary use of product composition data.

EPA also uses product composition data when reviewing applications for conditional registration. FIFRA § 3(c)(7)(A) authorizes the conditional registration of products which are "identical or substantially similar to any currently registered pesticide...or differ only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment..." In nearly every case, this determination involves an examination of an applicant's product and a comparison with the composition of currently-registered products.

Finally, EPA compares data on product composition with information on the composition of materials used in toxicity tests and other kinds of studies. This comparison indicates which ingredients in a pesticide product have been evaluated by a particular study, and might lead to a conclusion that another study is needed.

Based on its conclusions concerning the environmental characteristics and toxic properties of the pesticide, EPA can impose appropriate use restrictions, labeling requirements, special packaging requirements, or other needed requirements.

2. Physical and chemical characteristics. Data on the physical and chemical characteristics of pesticide chemicals and products are presented in §§ 63-2 through -21. These data are obtained from relatively simple and inexpensive measurements, observations, or tests. Some characteristics confirm or provide supportive information on the identity of ingredients and products. This is particularly true for determinations of color, odor, physical state, melting and boiling points, density, specific gravity, solubility, vapor pressure, and pH. In addition, such data provide information which is useful in reviewing the manufacturing or formulating process used to produce the chemical or product. Marked raising or lowering of pH, melting or boiling points, vapor pressure, density, specific gravity, or solubility, for example, may provide evidence of significant changes in manufacture or formulation, and could indicate the need to investigate product composition further.

Other information - color, odor, physical state, pH, and viscosity - is needed by the Agency to respond to emergency requests for identification of unlabeled pesticides involved in accidents or spills. Physicians, hospitals, and poison control centers also request such information from time to time when apparently-poisoned victims (or their families or acquaintances) cannot identify specific pesticide

products to which the victims have been exposed. This has often been the case when pesticides are removed from their original containers.

Certain other physical and chemical characteristics data are used directly in hazard assessment. These include stability, oxidizing and reducing action, flammability, explodability, storage stability, corrosion, and dielectric breakdown voltage. EPA requires a study of the corrosion characteristics of a pesticide to evaluate the effect of the product formulation on the container; if the pesticide is highly corrosive, then lids, liners, seams, or container sides may be damaged causing the contents to leak during storage, transportation, handling, or use. The storage stability study provides data on change (or lack of change) in product composition over time; if certain ingredients decompose, obviously other new chemicals are formed whose toxicity and other characteristics need to be considered. This situation is also true, to some extent, for data needed on stability of technical chemicals. Depending on the results of those tests, EPA may impose requirements for precautionary label statements.

Finally, certain data required in this series are needed as basic or supportive evidence in initiating or evaluating studies required by other disciplines. For example, the octanol/water partition coefficient is used as a criterion in determining whether certain fish and wildlife toxicity studies (in Subdivision E) must be conducted. Data on vapor pressure are used directly in determination of reentry intervals for products that may be used in situations where residues in air pose a potential hazard (Subdivision K). Data on viscosity and miscibility provide supportive information on tank mix proposals (examined more extensively in Subdivision N) and spray application instructions (of special concern in Subdivision H).

II. EXPLANATION OF APPROACH

This part of the Discussion explains the approach and concept of the Product Chemistry guidelines. After explaining terms that are used throughout the discussion and the guidelines, this part describes and explains the purposes of the specific major substantive requirements, beginning with the requirement to submit a statement of formula.

A. Definitions.

The Administrator is authorized by FIFRA to regulate pesticide products distributed in commerce. The term "pesticide product" is defined in 40 CFR 162.3(hh) as a pesticide which is offered for distribution and use; the term includes not only the pesticidal substance or mixture, but also the labeled container and supplemental labeling. The Product Chemistry guidelines divide all pesticide

products into two categories: "end-use products" and "manufacturing-use products." Section 60-2(b) defines end-use product 1/ as "a pesticide product intended to be labeled with instructions for direct use or application for pesticidal purposes." A "manufacturing-use product," defined in § 60-2(g), is "any pesticide product other than an end-use product." Thus, manufacturing-use products are, as the term implies, used in the production of end-use products, primarily through reformulation, i.e., mixing the manufacturing-use product with different chemical substances such as solvents or diluents to form new pesticide products. Usually manufacturing-use products contain a high concentration of the active ingredient. Such manufacturing-use products are often referred to as "technical grade products." The term "manufacturing-use product" also applies to products which are repackaged either into smaller containers or with different labeling.

All pesticides are composed of one or more substances. For regulatory purposes these substances are classified either as active ingredients, intentionally-added inert ingredients, or impurities. The term "active ingredient" is defined by FIFRA sec. 2(a) as:

> (1) In the case of a pesticide other than plant regulator, defoliant, or desiccant, an ingredient which will prevent, destroy, repel, or mitigate any pest;
>
> (2) In the case of a plant regulator, an ingredient which, through physiological action, will accelerate or retard the rate of growth or rate of maturation or otherwise alter the behavior of ornamental or crop plants or the produce thereof;
>
> (3) In the case of a defoliant, an ingredient which will cause the leaves or foliage to drop from a plant; and
>
> (4) In the case of a desiccant, an ingredient which will artificially accelerate the drying of plant tissues.

In short, the active ingredients in pesticides are the substances which directly produce the intended pesticidal effect.

FIFRA sec. 2(m) defines "inert ingredient" as "an ingredient which is not active." Inert ingredients are divided into two groups: those which are intentionally added to the pesticide and

---

1/ The term "end-use product" replaces the term "formulated product" used in the proposed Product Chemistry guidelines. [See § 40-2(b) of proposed Subpart B, and also § 30-2(b)(6) of current subdivision A.]

those which are not, i.e., impurities. Intentionally-added inert ingredients are any ingredients, other than active ingredients, which are intentionally included in a pesticide for some useful purpose. [See § 60-2(f).] Intentionally-added inert ingredients include wetting agents, emulsifiers, surfactants, aerosol propellents, diluents, solvents, stabilizers, and the like.

Finally, pesticides contain "impurities," substances "other than an active ingredient or an intentionally-added inert ingredient." [See § 60-2(c).] Impurities include such substances as unreacted starting materials, side reaction products, contaminants, and degradation products.

In recent years, EPA has become increasingly concerned about impurities in pesticides, particularly impurities associated with an active ingredient. The term "impurity associated with an active ingredient," defined at § 60-2(d), means:

> (1) Any impurity present in the technical grade of the active ingredient (e.g., a substance carried over from a beginning material, or from an intermediate, and impurities formed through side reactions or by degradation of the active ingredient); and
>
> (2) Those impurities which form in a pesticide product through reactions between the active ingredient and other substances in the product, or in the packaging of the product.

[The reasons for using this definition and for imposing stricter requirements on this group of impurities are explained in part III.A. of this Discussion.]

The definition of "impurity associated with an active ingredient" includes another term, "technical grade of the active ingredient," which also appears frequently in the Product Chemistry guidelines. This term [see § 60-2(i)], which is used interchangably with "technical chemical," means a material:

> which contains an active ingredient;...which is produced on a commercial or pilot plant scale (though it may never be held for sale); and...to which no inert ingredient has been deliberately added....

Finally, the Definitions section at § 60-2(e) defines the term "integrated formulation system" as:

> a process for producing an end-use product through the use of any substance which contains an active ingredient and which:
>
> (1) Is not a registered manufacturing-use product; or

> (2) Was produced or acquired in a manner that does not permit its inspection by the Administrator under sec. 9(a) of FIFRA, prior to its use in the process.

In other words, this term includes, but is not limited to, any process for producing a pesticide product that would contain an active ingredient which is not present as the result of using a registered pesticide product purchased from another. End-use products not produced by an integrated formulation system are unlikely to contain any impurities associated with an active ingredient other than those impurities already identified in connection with registration of a product used to make such an end-use product. The purpose, then, of including this definition is to distinguish between the two types of end-use products (those produced by an integrated formulation system and those which are not), and to allow the Agency to impose less stringent requirements on products which are not produced by such a system. (See parts II.E., F., G., and H. of this Discussion.)

B. The Formulators' Exemption.

FIFRA sec. 3(c)(2)(D) provides that:

> No applicant for registration of a pesticide who proposes to purchase a registered pesticide from another producer in order to formulate such purchased pesticide into an end-use product shall be required to -
>
> (i) submit or cite data pertaining to the safety of such purchased product; or
>
> (ii) offer to pay reasonable compensation otherwise required by [§ 3(c)(1)(D)] for the use of any such data.

This section, commonly called the "formulators' exemption" or the "horizontal line provision," relieves formulators of end-use products from the obligation to provide data concerning the safety of ingredients in registered pesticide products they purchase.

The formulators' exemption applies primarily in the physical and chemical characteristics portion of the Product Chemistry guidelines (§§ 63-1 through -21). Certain sections of that portion of the guidelines require data on the technical chemical to support the registration of both end-use products and manufacturing-use products. If an end-use product is manufactured by using a purchased, registered manufacturing-use product, the end-use product registrant is exempted by FIFRA sec. 3(c)(2)(D) from submitting physical and chemical property data on the active ingredient(s) in the manufacturing-use products. Similarly, if an applicant uses a purchased, registered, end-use product to produce his own end-use product, and the label of the applicant's product contains only uses which appear on the label of

the purchased product, the applicant is covered by the formulators' exemption. The primary result of the formulators' exemption is to lessen the data requirements for companies that simply use a registered pesticide to make their end-use products.

C. Statement of Formula.

The most important section in the Product Chemistry guidelines is contained in § 61-1, Product identity and disclosure of ingredients. This section discusses the submission procedures for the statement of formula identifying each active ingredient, each intentionally-added inert ingredient, and, in certain cases, impurities that may be present in the product while it is being distributed in commerce. Identification of an ingredient includes a variety of information: for all ingredients, the chemical name and Chemical Abstracts Service (CAS) number; for active and intentionally-added inert ingredients, the purpose or function of the ingredient; and for active ingredients, the molecular, structural, and empirical formulas, the molecular weight (or range), as well as other means of identification.

In addition to identifying the ingredients in his product, the applicant must also provide certified limits for the ingredients listed in the statement of formula. Upper and lower certified limits must be established for each active ingredient and each intentionally-added inert ingredient. In addition, for some types of products, an upper certified limit must be established for certain impurities. (See part II.G. of this Discussion.) The upper certified limit is the maximum (and the lower certified limit is the minimum) amount of the ingredient that will be present in the product at any time while it is in commerce.

Finally, § 61-1 requires an applicant to identify his product by the product name and trade name(s) (if different). In addition, the guidelines request (but do not require) the company code number assigned to the product.

The purposes of the requirements in this section are to obtain a comprehensive listing of the ingredients that may be present in a product and the amounts of such ingredients and to assemble in one section of an application all of the major types of identifying information on a product and its ingredients. The composition information will be used primarily in subsequent evaluations of the safety of the product. (See part I.D. of this Discussion.) The identifying information will be used as an aid in locating data in the public literature concerning the human health and environmental properties of the product and/or its ingredients.

D. Description of Beginning Materials and Manufacturing Process.

Most of the other sections of the Product Chemistry guidelines are intended to produce data to support the information contained in

the statement of formula required by § 61-1. The first of these data requirements are contained in § 61-2, concerning descriptions of beginning materials and the manufacturing process.

The most basic pieces of information needed to determine the composition of a pesticide product are the identity and, so far as feasible, the composition of the materials used to produce the product. Section 61-1(a) requires an applicant to identify each "beginning material" 2/ used to produce his product and to supply certain information (if available to the applicant) on the beginning material. Specifically, the applicant is required to submit a copy of available technical specifications by which the supplier of a beginning material describes its composition, properties, and/or toxicity as well as any other information available to the applicant concerning the composition of the beginning material. If a beginning material is a registered pesticide product, it is sufficient simply to identify the product by its registration number.

The requirements concerning the description of beginning materials represent a significant change from the proposed Product Chemistry guidelines. In the proposal, an applicant would have been required to provide "the identity and the percent composition by weight of each substance present in the material [and] the expected variation in composition (to the extent that this information is reasonably ascertainable)..." Not only was this proposed requirement vague, but it could also have been interpreted as requiring applicants to perform difficult and expensive chemical analyses of beginning materials. To eliminate these potential problems, the Agency rewrote the section to state that an applicant is required to submit only the information (of the types specified) which is available to him. The section does not require an applicant to perform periodic chemical analyses of his beginning materials.

The next kind of information necessary to evaluate the composition of a pesticide is a description of the manufacturing process used to make the product. Section 61-2 specifies the kind of information which should be contained in this description. Among other things, the description should include: a statement of the order in which beginning materials are added and their relative amounts; a description of the physical conditions controlled during the manufacturing process; a description of any purification procedures; and a description of any quality control measures. In addition, the applicant must provide a flow chart showing the intended chemical reactions occurring during each step of the process.

2/ The term "beginning material" is defined in § 60-2(b) and means replaces "starting material" which is generally understood to apply only to raw materials. As used in the Product Chemistry guidelines, "beginning material" has a broader meaning; it includes all materials, whether raw or processed, used in the manufacturing or formulating process.

Together, the descriptions of beginning materials and of the manufacturing process identify the major variables affecting the composition of a pesticide product. EPA's chemists can review this information along with information required by other sections to determine whether the applicant's product will contain the ingredients and conform to the certified limits listed in the statement of formula.

E. Discussion of the Formation of Impurities.

Section 61-3 addresses the applicant's submission of a discussion based on chemical theory of the impurities that may be present in his pesticide products and to explain how such impurities may be formed. Applicants are required to address impurities which either have been detected by analysis of samples of the product or are expected to be present in quantities equal to or greater than 0.1 percent of the product.

EPA expects the theoretical discussion to serve several functions. EPA will learn what kinds of impurities the applicant expects will be present in his product as it is distributed in commerce. EPA can independently evaluate this information to determine whether other impurities might be present in the product. In addition, the thoroughness of the theoretical discussion can indicate how reliable other pieces of information supplied by the applicant might be. Finally, the list of impurities generated by the theoretical discussion becomes the basis for the sample analysis requirements contained in 40 CFR § 158.24.

This section of the guidelines states expressly that the discussion is to be based on the information concerning beginning materials and manufacturing process required by § 61-2. It also specifies the particular kinds of chemical reactions which must be considered and discussed. Different requirements in this latter respect are established for end-use products not produced by an integrated formulation system and all other products (end-use products produced by an integrated formulation system and manufacturing-use products). See § 61-3(b)(1) and (c)(1). Applicants seeking to register end-use products not produced by an integrated formulation system are subject to less stringent requirements since the impurities associated with an active ingredient in such a product will almost always be the impurities present in the pesticide products used to manufacture their products. Thus, for these applicants, the theoretical discussion should focus on possible reactions between the active ingredient and other ingredients in the pesticide when such information is known. Applicants seeking to register other kinds of products must discuss the possibility of chemical reactions involving other substances, e.g., reactions between intentionally-added inert ingredients.

F. Results of Preliminary Analyses.

Section 62-1, concerning preliminary analysis of product samples, is intended to allow an applicant to confirm the conclusions reached in the theoretical discussion. This section requires applicants to report the results of analyses of a representative set of samples (at least five) of the product. The analyses must be designed to measure the amount of active ingredient present in the product and to identify and quantify (if present) any impurity associated with an active ingredient which is expected (based on the theoretical discussion) to constitute 0.1 percent or more of the product. On a case-by-case basis EPA may require applicants to analyze product samples for other ingredients or to provide identifying spectral data.

The requirements for analysis of product samples apply only to manufacturing-use products and end-use products produced by an integrated formulation system. Once again, end-use products not produced by an integrated formulation system are subject to less stringent requirements. Applicants seeking to register such products will be required to provide the results of sample analysis only on a case-by-case basis.

Applicants are permitted to use any analytical method they consider appropriate. The analytical methods used to satisfy the requirements of this section will not be evaluated by the more rigorous standards concerning reproducibility, accuracy, and precision applicable to the "verification" methods required by § 62-3. Applicants are, however, required to describe each method in detail and to state its precision and accuracy.

G. Certified Limits.

Section 62-2 requires applicants to explain how they determined the certified limits for the ingredients in their products. In addition, this section establishes certain requirements concerning certified limits and explains that certified limits are used in two ways. First, EPA reviews the composition of pesticide products to determine whether the product will cause unreasonable adverse effects on the environment. This review will involve, among other things, an evaluation of the upper bound of the toxicity of a product, that is, the toxicity of a product if the most hazardous ingredients were present in the product at the upper certified limits set for such ingredients. Second, certified limits will become the basis for future enforcement actions. FIFRA sec. 12(a)(1)(C) states that it is unlawful to sell or distribute:

> any registered pesticide the composition of which differs at the time of its distribution or sale from its composition as described in the statement required in connection with its registration under section 3.

The "statement required in connection with its registration" is the statement of formula required by § 61-1. Once a statement of formula containing certified limits has been submitted for a product, each quantity of the pesticide in commerce must conform to the composition described in the statement of formula (i.e., the amount of each ingredient must fall within the certified limits) or the product will be considered in violation of FIFRA sec. 12(a)(1)(C).

The section states that a certified limit is valid as long as the product is in commerce or until a specific expiration date stated on the label. Thus, an applicant needs to predict how long his product is likely to remain in commerce and what storage conditions may occur during that period. Based on this information and his knowledge of chemistry, the applicant then needs to establish certified limits that take into account possible degradation of the product's ingredients. If an applicant expects his product to contain one or more ingredients that degrade rapidly, the applicant can place a specific expiration data on the label of the product and a statement that the product shall not be used after that date.

In response to public comments, EPA has added a new paragraph, § 62-2 (a)(4), to this section specifically asking applicants to set, for intentionally-added ingredients and impurities, limits based on a consideration of product variability. The limits stated should not greatly exceed those actually occuring in the product when normal quality assurance procedures are used in the production process. At the same time, the stated ranges should define product composition sufficiently for the Agency to determine its suitability for registration.

Finally, this section specifies the ingredients for which certified limits are required. For manufacturing-use products and those end-use products produced by an integrated formulation system, the applicant must report upper and lower certified limits for active ingredients and intentionally-added inert ingredients and upper certified limits for impurities associated with an active ingredient which were found or theorized to be present in quantities equal to or greater than 0.1 percent of the product. Once again, for reasons discussed earlier, end-use products not produced by an integrated formulation system are subject to less stringent requirements. These products are only required to provide upper and lower certified limits for active and intentionally-added inert ingredients; upper certified limits for the impurities in those products are not routinely required. Of course, on a case-by-case basis EPA may require additional certified limits.

H. Methods to Verify Certified Limits.

Section 62-3 requires applicants to submit an analytical method for detecting and measuring the quantity of each active ingredient (and certain impurities) in their products. These methods must be capable of determining whether the ingredient falls within its certified limits and also be suitable for use in state federal enforcement programs. Therefore, the applicants must submit data to establish the precision and accuracy of these methods.

Since such methods can usually be adapted to formulated products, the requirement for verification methods applies only to manufacturing-use products and end-use products produced by an integrated formulation system. As with other requirements, EPA may require, on a case-by-case basis, methods for additional ingredients (e.g., low level impurities or intentionally-added inerts) or additional products (e.g., end-use products not produced by an integrated formulation system).

In response to public comments, EPA has added paragraph (b)(3)(iii) of § 62-3 to provide guidance on the precision of verification methods. The guidance is based on the standards generally endorsed by the American Association of Official Analytical Chemists (AOAC); these standards, merely reflect the prevailing state of the art in analytical chemistry. In any case, EPA stresses that the paragraph only contains guidance; it does not establish criteria that will automatically result in rejection of a method which does not achieve the recommended precision.

I. Physical and Chemical Characteristics.

Sections 63-1 through -21 contain requirements to submit data on the physical and chemical characteristics of a pesticide product and its ingredients, particularly the active ingredient. These data requirements are subject to the formulators' exemption contained in FIFRA sec. 3(c)(2)(D). (See part II.B. of this Discussion.) These requirements have a variety of purposes. Some characteristics, such as explosiveness and flammability, are directly related to hazards to humans. EPA requires data on other characteristics, e.g., solubility and viscosity, to assess the behavior of the product when it is used. Still other properties like color, density, and odor are used to identify the pesticide in emergency situations. Finally, some characteristics, such as melting and boiling points, are relevant to the review and evaluation of the manufacturing process.

The Agency requires applicants to add warning statements to their product labels on the basis of these physical and chemical characteristic. Some of the labeling requirements appear in 40 CFR 162.10(h)(2)(iii), and others will appear eventually in proposed labeling regulations. EPA may also require changes in use directions based on the results of physical and chemical characteristic tests.

For the most part, the physical and chemical characteristics covered by these sections are determined routinely for all pesticide Products. Moreover, these characteristics are usually determined with testing techniques which were standardized years ago and are now widely used. Each of these guidelines sections contains a "References" paragraph which cites standardized testing techniques, usually published by the Organization of Economic Cooperation and Development (OECD) and the American Society for Testing and Materials (ASTM). While EPA recommends that these protocols be used, EPA will accept determinations made using other techniques, so long as the techniques are validated and the specific test standards in the appropriate sections are satisfied.

J. Submittal of Samples.

The last section of the Product Chemistry guidelines is § 64-1. Titled Submittal of samples, this section requires that a sample of an analytically-pure grade of each active ingredient and the technical grade of each active ingredient in a product be submitted to EPA. It is usually sufficient for only one applicant to submit the analytical grade sample, and for all other applicants seeking to register a pesticide product containing that active ingredient to rely on the first applicant's submission. However, the same approach does not work with regard to submission of technical chemicals. Each and every producer of a technical grade of an active ingredient (TGAI) is required to submit a sample and each applicant must specify which TGAI is used to formulate his product.

The purpose of the requirements to submit samples is for EPA to have a small quantity of a known substance which EPA can then use in validating its enforcement results and in making comparisons between similar products manufactured by different producers.

K. Timing of Data Submissions.

Information on the composition of a pesticide product is essential for EPA to decide whether to approve applications to register pesticide products. Ideally, before approving a registration, EPA would like to receive all of the information required by these Product Chemistry guidelines based on the the product as it will be distributed in commerce. Practically, however, this is not always feasible, particularly when a company is seeking to expand its production into a new type of pesticide.

Section 60-3(a) states that product chemistry data shall be derived from testing with commercially-produced pesticides. Yet when a company is developing a new pesticidal active ingredient or trying to enter the market for a registered active ingredient, the company may be unwilling to build commercial-scale facilities until EPA has

approved its application for registration. In such cases, the applicant's product chemistry data could only be based on material produced on a pilot scale. EPA will accept such data for purposes of evaluating applications as provided in § 60-3(c). If registration is granted, EPA will also impose requirements and a schedule for submitting data based on commercial production.

The conditional registration program authorized by FIFRA sec. 3(c)(7) also affects the timing of product chemistry data submissions. In general terms, the conditional registration program allows EPA to approve the registration of a product even though the application does not contain (or reference) all of the data needed by EPA to determine whether the pesticide would cause unreasonable adverse effects on the environment. Instead, EPA needs to determine that the applicant's product is the same as, or is substantially similar to, a currently-registered product [FIFRA sec. 3(c)(7)(A)] or that it only proposes to add a new use to those already approved for currently-registered products [FIFRA sec. 3(c)(7)(B)].3/ In either case, EPA must also determine that use of the applicant's product would not substantially increase the risk of unreasonable adverse effects.

FIFRA sec. 3(c)(7) provides generally that EPA may issue conditional registrations without requiring applicants to submit data that current registrants of similar products have not been required to submit. Many current registrants have not submitted data which would satisfy these Product Chemistry guidelines. Thus, EPA is authorized to issue conditional registrations without first obtaining comprehensive product chemistry data, so long as it has adequate information to make the statutorily-required determinations. The Agency has concluded, however, that the information on product composition is necessary to determine whether an applicant's product is identical or substantially similar to a currently-registered product. Therefore, EPA has decided to require applicants for conditional registration to provide most of the data specified in these guidelines. The existing regulations on conditional registration, 40 CFR § 162.18-2(c)(1) and (d)(1), establish requirements for product chemistry data, and § 60-1(c) of the Product Chemistry guidelines describes those requirements.

3/ In certain limited circumstances, FIFRA sec 3(c)(7)(C) allows EPA to register products containing active ingredients not present in any previously-registered product.

III. ISSUES IN PRODUCT CHEMISTRY

Many useful comments were supplied to the Agency as a result of the proposal of the Product Chemistry guidelines in 1978. These comments suggested many changes to improve the proposal and identified issues that had to be resolved before these guidelines could be published. Additional issues and further upgrading were evident during internal Agency review and revision of these guidelines. In responding to these issues, the Agency has generally developed less burdensome requirements than were originally proposed, has required data and information that applicants could more easily obtain, and has clarified those requirements which commenters found ambiguous. At the same time, EPA has established requirements which will provide product chemistry information that is adequate to assess the safety of pesticides.

The major issues raised by reviewers of the proposed Product Chemistry guidelines involved the following general topics:

- Information on impurities.
- Submittal of a theoretical discussion on formation of impurities.
- Development of certified limits for product ingredients and impurities.
- Submittal of information on manufacturing process.
- Submittal of analytical methods.
- Timing of submittal of certain data.

A. Information on Impurities, and Discussion on Their Formation.

The 1978 guidelines proposed several requirements specifically aimed at better delineation of unintentional substances in pesticide products, including (principally) impurities, reaction products, and degradates. These requirements were developed as a result of finding dioxins, ethylene thiourea, N-nitrosamines, and several other hazardous substances as impurities or degradates in a number of widely-used pesticide products. The proposed guidelines required, among other things:

- A discussion on formation of unintentional ingredients in a product;
- A declaration and certification of upper limits for each impurity, reaction product, and degradate known to be present or reasonably identifiable as present in the product;

- Analytical methods for detecting and measuring each identifiable impurity present in quantities of 0.01 percent (of the weight of the product) or more;

- A statement of formula identifying each reasonably identifiable substance in the technical chemical and listing the presence of each by percentage weight or as ppm; and

- Name and structural formula (if available) for each impurity, reaction product, or degradate.

These proposed requirements elicited many comments. The major issues and the Agency response and action to each are explained below.

1. Information on impurities. Comments - Concern was expressed about what is "reasonably identifiable"; that it was impossible to satisfy the identification requirements in some cases, and that, in many other cases, such identification information was not particularly useful. Some commenters stated that the number of chemicals which might be "reasonably identifiable" is exceedingly large, and that EPA should not require extensive identifying information on such a potentially long list of substances. There was concern that many small and medium-sized formulators would be unable to afford the costs of determining the identifying information required by the guidelines. A suggestion was offered that routine analysis of such product conponents should be at the 0.1 percent level rather than at the 0.01 percent level, and that additional analyses to determine whether other components were present should be required only when the impurities are highly toxic.

Responses - In response to these concerns and comments, the Agency made a number of significant revisions in the guidelines. In addition, EPA has provided more comprehensive explanation of those proposed requirements that were retained for the current guidelines. A discussion of the actions taken and the reasons for retaining certain of the proposed requirements is provided in the following paragraphs.

EPA has concluded that there is no reason to require a characterization of the technical grade of each active ingredient to support the registration of a pesticide product and accordingly has deleted the provision which is the subject of some of the above comments. The requirement was included in the proposed product chemistry guidelines as an indirect way of identifying some of the impurities which were associated with the active ingredient. A number of changes in the guidelines have been made that improve the nature of this data requirement without requiring more data than are actually needed for Agency review and decision-making.

One of these changes was instituted by directing attention to impurities associated with the active ingredient, the major source of toxicity in most pesticide products. In order to clarify which impurities are considered associated with an active ingredient, EPA has added to the current product chemistry guidelines a definition of the term "impurity associated with an active ingredient." [See § 60-2(f) and the explanation provided in the Discussion at Part II.A.] The description of the manufacturing process addressed by § 61-2 and the discussion of the formation of impurities addressed by § 61-3 still provide the basis for determining which impurities fall within the scope of the above definition.

In response to the comments about the volume and value of data that could be generated to meet some of the requirements regarding impurities, the Agency agrees that the proposed guidelines would have required identifying information on a long list of substances, some of which were never likely to be in a pesticide product and others of which would be present in very small toxicologically-insignificant amounts. The Agency recognizes that the proposed requirement would have been burdensome and that it would have provided information which would be only occasionally useful to the Agency.

Accordingly, the Agency now requires identifying information on substances "which might reasonably be identifiable as present in the pesticide product...and those reaction products and degradation products known or theorized to be formed..." The primary purpose of the requirement to provide identifying information is to make available for easy reference and use by the Agency a nearly complete list of the different ways a chemical substance is identified. The Agency can then use these different pieces of information to collect additional knowledge about the effects of the substances, principally through computerized literature searches. The Agency now requires identifying information only for those ingredients for which a certified limit must be established. (See § 61.1(b) of the current guidelines.) Basically, the Agency now requires certified limits (and thus identifying information) only for two groups of product components:

- Those ingredients (active and inert) deliberately included in the product; and

- Those impurities which are present in quantities greater than 0.1 percent or, if less, present in potentially hazardous amounts.

These requirements encompass relatively few product components compared to all "reasonably identifiable" components for which limits would have been required in the 1978 proposed guidelines.

The Agency's approach is that, in addition to active ingredients and intentionally-added inert ingredients, the requirement applies to impurities which are expected to be present in the pesticide and which are potentially hazardous because they are associated with the active ingredient.

The revision of proposed § 163.61-3(c) (now § 61-1(b) in the current guidelines) imposes far fewer requirements on the formulator of an end-use product than the proposal. Under the current guidelines, most formulators will only need to supply identifying information on the intentionally-added inert ingredients in their product. The Agency thinks such identifying information is readily available. Thus the requirements for statement of formula should no longer be considered burdensome. A more detailed explanation follows regarding the new requirements in relation to types of impurities in manufacturing-use products and in end-use products of the typical type and those produced by an integrated formulation system.

One of EPA's primary concerns in developing the product chemistry guidelines is to require information which permits the Agency to evaluate the possible hazards of impurities associated with the manufacture of the active ingredients in pesticide products. In particular, the Agency has concluded that it needs to know both the identity of such impurities and the amount of each impurity in a product. In contrast, the Agency is not ordinarily concerned about the identity or amount of impurities which are associated with the intentionally-added inert ingredients in a product.

There are two reasons for treating the two classes of impurities differently. First, EPA's historical experience is that most of the impurities in pesticide products which have presented risks to humans and the environment have been associated with the pesticidally-active ingredients. For example, TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin), one of the most toxic chemicals known, is an impurity produced in the manufacture of the herbicide 2,4,5-T. Ethylene thiourea (ETU), a known carcinogen, is a degradation product of the active moiety ethylene(bis)dithiocarbamate present in several widely used fungicides. Second, and perhaps more importantly, chemical theory suggests that chemically similar substances are often likely to produce similar biological effects. Since active ingredients are intended to kill, repel, or otherwise significantly affect biological organisms, it follows that impurities which are associated with such ingredients may also be biologically active.

To understand the difference in requirements for the two classes of end-use products, it is also necessary to note the requirements imposed on manufacturing-use products. The registration application for manufacturinguse products must contain a certified upper limit for each impurity associated with an active

ingredient present in quantities greater than 0.1 percent. (See § 62-2(b) of the current guidelines.) The guidelines may also require an analytical method to verify each such limit. [See § 62-3(b)(1) (iii) of the current guidelines.]

With this information, it is easy to understand why EPA imposes less stringent requirements on end-use products which are not produced by an integrated formulation system. Simply, those end-use products, by definition, are manufactured or formulated from manufacturing-use products over which the Agency has adequate control. Thus, end-use products not produced by an integrated system normally would not contain any impurities associated with the active ingredient except those introduced from the manufacturing-use product. If needed, the Agency could in most cases calculate the percentage of such impurities in the end-use product based on the quantity of the impurities in the manufacturing-use product and the amount of the manufacturing-use product used. Similarly, the Agency can often adapt the analytical methodology developed for the manufacturing-use product for use on the end-use product. Accordingly, little purpose would be served by imposing on registrants of end-use products not produced by an integrated formulation system the requirements for data on the manufacturing impurities associated with an active ingredient.

End-use products produced by an integrated formulation system, however, contain active ingredients whose presence in the product is not the result of using a purchased manufacturing-use product. Consequently, the Agency has no indirect method of controlling the amount of impurities contained in these products. Therefore, the Agency imposes the requirements to certify an upper limit for each impurity associated with an active ingredient and to develop analytical methods to verify the limits. In short, imposing these requirements on end-use products produced by an integrated formulation system is the only way the Agency has to obtain the information it needs to evaluate the safety of these products.

Finally, the Agency notes that these requirements really are not as burdensome as some commenters suggest. Most manufacturers who use an integrated formulation system also produce manufacturing-use products containing the active ingredients which are present in their end-use products. Most, if not all, of the effort required to develop the information to support the registration of the end-use product would be needed to produce the information which supports the registration of the manufacturing-use product. Thus, in most cases, little additional expense results from these requirements.

2. Theoretical Discussion. Comments - A great many comments were directed at the requirement for theoretical discussion on the formation of impurities. Some felt that EPA lacked the legal authority to require a discussion on formation of unintentional ingredients except when such ingredients created a threat to human health or

the environment and that, instead, the Agency should shift the emphasis to formation of active ingredients and intentionally-added ingredients and focus on known reactions and processes. Several felt the amount of theorizing about possible reactions is unlimited and could lead to fruitless disputes with the Agency over the completeness of the discussion. Moreover, applicants who use materials purchased from other chemical companies felt they would never be able to provide a satisfactory theoretical discussion because they would not know the complete composition of the materials they use; therefore, they argued that the requirement for a theoretical discussion should not be imposed on companies which formulate end-use products. They argued further that the requirement is inconsistent with the "formulators' exemption" in FIFRA sec. 3(c)(2)(D). Finally, commenters argued that, because of the relationship between the theoretical discussion and other requirements in the proposed guidelines (e.g., sample analysis and certified limits), applicants would be required to produce large amounts of expensive and relatively useless information.

Responses - [The Agency refers the reader to part I.A. of the Discussion on Subdivision A for a more thorough discussion of legal authority.] The Agency considers it has the legal authority, to require applicants to provide a discussion of the formation of unintentional ingredients, i.e., impurities. As is clear from the statute and legislative history, the applicant for registration of a pesticide bears the burden of proving that the product is safe, and that its use will not cause unreasonable adverse effects on the environment. [See FIFRA sec. 3(c)(5) and Sen. Rep. No. 838, 92nd Cong. 2nd Sess. p 20 (1972).] The commenter's approach would force the Agency to prove that a pesticide presented a risk, rather than requiring the applicant to provide data showing the absence of an unreasonable risk. This is clearly not the intent of the Act or of Congress. Also, the suggested approach implies that the Agency would need to know whether a product presented a risk before the Agency could require data to evaluate the potential of a risk. This is illogical, for if the Agency could prove that a risk existed, it would not need to direct the applicant to supply data to evaluate that risk.

The Agency rejects the suggestion to deemphasize the formation of impurities in pesticide products. EPA - and the public - is aware that there are a substantial number of human health and environmental hazards attributable to the presence of impurities in pesticides. For example, EPA is currently conducting cancellation hearings on the use of the herbicide 2,4,5-T because (among other things) it contains the highly toxic impurity TCDD. EPA has also directed the registrants of certain products to examine whether certain N-nitrosamines are present in their products.

The Agency expects the theoretical discussion to serve several functions. One can learn from it the kinds of impurities expected to be present in a product as it is distributed in commerce. The Agency can independently evaluate this information to determine whether other impurities might be present in the product. In addition, the thoroughness of the theoretical discussion can indicate how reliable other pieces of information supplied by the applicant might be. Finally, the list of impurities generated by the theoretical discussion becomes the basis for the sample analysis requirements contained in § 62-1.

With regard to the comment about "unlimited theorizing" leading to "fruitless disputes...over the completeness of the discussion," the Agency agrees in part with the comment. Proposed § 163.61-5 would have required the applicant to provide a theoretical discussion concerning the formation of unintentional ingredients that "might reasonably be identifiable as present" in the applicant's product. Critics interpreted this language to require an exhaustive discussion of virtually every known chemical reaction - however unlikely - which might occur. Since virtually every chemical is "identifiable" if proper analyses are performed, the proposal was understood to require unlimited discussion.

The Agency recognizes that the language of the proposed requirement was ambiguous, and that, if it were applied as some of the critics interpreted it, the requirement would be quite burdensome. Not only would the scope of the theoretical discussion be enormous, but the additional burdens, dependent on the list of impurities theorized to be present, would also be overwhelming.

Rather than try to resolve questions about the proper scope of the theoretical discussion through case-by-case review of applicant submissions, the Agency has revised this provision. (See § 61-3 of the current guidelines.) First, the theoretical discussion is now limited to impurities which may be present in quantities equal to or greater than 0.1 percent (1000 ppm). Thus, an applicant will not need to address possible reactions that might produce a few parts per million of an impurity, an amount which under the proposed guidelines might "reasonably be identifiable." Second, the Agency has listed the specific factors which must be considered in a theoretical discussion. [See § 61-3(b) and (c) of the current guidelines.] The factors are very broad, including, for example, migration of components of packaging material into the product, carryover of impurities in the beginning materials into the final product, and possible side-reactions during the manufacturing process. Despite the breadth of these requirements, the list does clarify and narrow the scope of the theoretical discussion. The Agency expects that the combination of a specific cutoff quantity,

0.1 percent, and a list of factors to address in the discussion will eliminate most of the ambiguity found in the proposed version of this requirement.

The Agency also agrees with the comments concerning the difficulty of providing a complete theoretical discussion when there is limited information available on the composition of beginning materials. Accordingly, the Agency has revised that section in the current Subdivision D guidelines to provide that the theoretical discussion "shall be based on established chemical theory and the information submitted under § 61-2 concerning the beginning materials and the manufacturing process used to make the product." Section 61-2, in turn, requires an applicant to submit only that information which is readily available on the composition of the beginning materials. Thus, the theoretical discussion requirements in the current guidelines accommodate many of the critics' concerns.

The Agency also agrees in part with the suggestion to impose less stringent requirements for a theoretical discussion on an applicant seeking to register an end-use product than on an applicant seeking to register a manufacturing-use product. The current guidelines have therefore been revised accordingly. For purposes of establishing requirements for a theoretical discussion, EPA divides pesticide products into two groups:

- Manufacturing-use products and end-use products produced by an integrated formulation system; and

- End-use products not produced by an integrated formulation system.

Persons seeking to register products in the latter group can provide a less rigorous and less thorough theoretical discussion than those seeking to register products in the former group. In general, the difference between the two sets of requirements is that a "non-integrated" formulator needs to address only the possible carryover of impurities in the beginning materials and the formation of impurities by chemical reactions involving the active ingredient or by degradation of an active ingredient. People seeking to register the other kinds of products must provide this information and discuss, in addition, the possible formation of impurities as the result of degradation of, or chemical reactions involving, substances other than active ingredients. [See § 61-3(b) and (c) of the current guidelines.]

The Agency, however, disagrees with the suggestion to require no theoretical discussion for end-use products. The commenter may have misinterpreted the Congressional intent of the 1978 amendment to FIFRA at sec. 3(c)(2)(D). The amendment provides that a registrant of an end-use product is exempt from the requirement to submit data

pertaining to the safety of any registered pesticide product purchased from another and used to manufacture his product. While this provision does reflect a Congressional purpose to reduce the burden on registrants of end-use products, it does not exempt them from requirements which uniquely pertain to the safety of their products. Since the provision concerning a theoretical discussion requires an examination of the possible formation of impurities during and after the manufacture of the end-use product, the data uniquely pertain to the end-use product and hence are not covered by FIFRA sec. 3(c)(2)(D).

In addition to revising the requirements concerning the discussion of the formation of impurities, the Agency has also modified the relationship between the theoretical discussion and other sections of the product chemistry guidelines. For example, instead of requiring applicants for registration of manufacturing-use products to analyze samples of their products for each impurity listed in the theoretical discussion (see proposed § 163.617), EPA has narrowed the requirement considerably. Thus, § 62-1 of the current guidelines requires an applicant for registration of a manufacturing-use product or an end-use product produced by an integrated formulation system to analyze his product for the presence of each impurity associated with an active ingredient which is theorized to be present in a product in quantities equal to or greater than 0.1 percent. No analysis is routinely required for impurities not associated with an active ingredient or expected to constitute less than 0.1 percent of the product. Moreover, analysis is not routinely required for end-use products not produced by an integrated system. Thus, in the current guidelines, requirements concerning sample analysis are no longer as heavily dependent on the theoretical discussion as they were in the proposal.

EPA has made similar changes in the section concerning certified limits. Instead of requiring a declaration and certification of limits for each impurity theorized to be present (see proposed § 163.61-6), the current guidelines require upper certified limits for impurities associated with an active ingredient which were theorized or found to be present in the product in quantities greater than 0.1 percent. This requirement applies only to end-use products produced by an integrated formulation system and to manufacturing-use products. End-use products not produced by an integrated formulation system are not routinely required to establish upper certified limits for impurities. If needed, the Agency could, in most cases, calculate the percentage of such impurities in the end-use product based on the quantity of the impurities in the manufacturing-use product and the amount of manufacturing-use product used. In summary, the Agency has revised the guidelines to reduce the burdens that would have been created by the overly broad requirements concerning discussion of impurities and other related provisions in the proposal.

B. Information on Manufacturing Process.

The requirement for a description of the manufacturing process in proposed § 163.61-4 asked for identification of starting materials and intermediate materials, as well as details of the process itself. This proposal elicited many comments challenging the overall approach as well as details of the requirements. Some of these comments and EPA's responses and actions are discussed below.

Comments - Some commented that EPA would not be able to use the information describing the manufacturing process and identifying starting materials. They also argued that data on beginning materials is trade secret information and, therefore, should not be required. Moreover, it was argued that data on the composition of beginning materials would be irrelevant to EPA, since the impurities in them are removed during manufacture and purification processes. Some felt that to isolate and analyze intermediate materials would be unreasonable and expensive. Many considered that registrants, upon meeting these requirements, would tend to be "locked" into a single manufacturing process, and thus development of more efficient processes would be discouraged.

Responses - The purpose of requiring information on the composition of materials used to produce a pesticide is to make the information available for Agency use in assessing the ingredients which are likely to appear in a marketed product. The EPA staff which will be assigned to review product chemistry data includes a number of scientists who, by virtue of their training, education, and experience, are skilled at predicting the ingredients which could be formed by chemical reactions between beginning materials, by degradation of substances, or through other mechanisms. The starting point for the analysis leading to such predictions, obviously, is a knowledge of what substances will be used to manufacture or formulate the pesticide. Thus, the information on beginning materials is necessary and very useful in evaluating the safety of a pesticide.

Many producers are not fully aware of the composition of beginning materials used to formulate or manufacture their products. In particular, suppliers of inert ingredients are usually very reluctant to provide detailed information on the composition of their chemicals. Because of the difficulty that would be involved in obtaining detailed information on the composition of beginning materials, EPA decided to revise proposed § 163.61-4 (now § 61-2(a) in the final guidelines). EPA revised the section to require an applicant to submit any information he has concerning the composition of the beginning materials. The revised provision does not require applicants to analyze samples of beginning materials or to request the supplier of a beginning material to send information to EPA.

The Agency disagrees, however, with the assertion that information on impurities in the beginning materials is irrelevant because the impurities are removed during manufacture. The Agency thinks that it is not uncommon for some products to contain impurities which carry over from the beginning materials into the final product. Moreover, it is important to know what impurities an applicant is trying to remove so that the Agency can assess the appropriateness of any purification procedures for removing such impurities.

The Agency has deleted the requirements for data on intermediate materials. The possibility that these materials might remain in the product as marketed must be addressed as part of the discussion on the formation of impurities required by § 61-3 of the current guidelines.

FIFRA authorizes EPA to require submission of trade secret information which is necessary to evaluate the safety of a pesticide product. (See secs. 3 and 10 of the Act.) The statute also requires that trade secret information generally may not be disclosed to the public and establishes severe criminal penalties for any Federal employee who discloses trade secret information. [See FIFRA sec. 10(f).] The current product chemistry guidelines indicate in § 60-3(e) that information required by the guidelines will be treated as trade secrets to the extent provided by FIFRA sec. 10. EPA has established strict internal procedures to ensure that trade secret information is not inadvertently released. Finally, the Agency has been receiving and reviewing trade secret information for years and believes that the combination of statutory sanctions and internal procedures has provided (and will continue to provide) adequate protection for trade secret information submitted to the Agency.

The Agency disagrees with the comment that the requirement of proposed § 163.61-4(b) would "lock" a producer into using a specific manufacturing process. To clarify this view, however, EPA has added a new paragraph to the current guidelines which explains what a registrant is required to do if he wants to change the manufacturing process. The new paragraph, at § 61-2(c), states, in part:

> (c) Changes in beginning materials or manufacturing process. Any registrant who changes his beginning materials, who discovers additional information concerning his beginning materials, or who changes his manufacturing process must report that information to the extent required by FIFRA sec. 6(a)(2). If the change or information indicates that the certified limits established in accordance with § 62-2 no longer apply to the product, the registrant must apply to amend the registration of his product to establish new certified limits.

This paragraph allows a registrant to change his beginning materials or his manufacturing process whenever he wants. If the changes would be pertinent to whether the terms of the registration of the product should be modified, or to whether the product's registration should be cancelled or suspended, the information regarding the change must be reported. [See "Enforcement Policy Regarding Failures to Report Information under Section 6(a)(2) of the Federal Insecticide, Fungicide and Rodenticide Act," 44 FR 40716 (July 12, 1979)]. In addition, if the changes would produce products with a composition that no longer conformed to the certified limits established for the product, the registrant would be required to amend his registration to set new limits.

EPA expects that many, perhaps most, changes in the manufacturing process would not be required to be reported under § 61-2(c). Likewise, because EPA will permit reasonable variation in the amount of an ingredient in a product, the Agency expects very few of the changes in a producer's manufacturing process will necessitate a revision of certified limits. Finally, even if a registrant must amend his registration to certify slightly different limits for a product produced by a new process, the Agency will probably approve the amendment without delay. Thus, the Agency thinks that the requirements in the product chemistry guidelines will only inhibit registrants from making changes that would lead to major differences in the composition of the product. The Agency does not expect that registrants will be prevented or even significantly discouraged from making minor changes.

C. Certified Limits.

EPA proposed in § 163.61-6 that applicants declare and certify ingredient limits for their products. For each active and intentionally-added inert ingredient, both upper and lower limits would be required, and for each identifiable impurity, reaction product, or degradate, an upper limit. For each limit, the applicant would explain how the limit was established, and show how much of each ingredient was in the product.

Comments - Comments on this proposal ranged from questioning the legality of the proposal to suggesting several alternative ways to obtain certified limits through modification of some of the aspects in the requirements. One comment stated that EPA lacked the legal authority to require applicants to establish certified upper and lower limits for pesticide ingredients unless there is a specific need for certified limits for these on a given product to protect human health or the environment. Others felt that the requirement for certified limits for every ingredient which might be "reasonably identifiable" was inappropriate for many products, especially since the amounts of many minor ingredients are exceedingly difficult to

control. Therefore, a number of suggestions were offered as alternatives to the requirement for certified limits in proposed § 163.61-6:

- (a) Require certified limits only for biologically-active ingredients present in toxicologically-significant amounts;

- (b) Require certified limits only for ingredients identified by the Occupational Safety and Health Administration (or some other government body) as constituting "potential safety hazards";

- (c) Require certified limits only for "major active ingredients," i.e., the technical chemicals intentionally added to a pesticide product from which a specific pesticidal response is expected;

- (d) Require certified limits only for active ingredients, intentionally-added inert ingredients, and impurities appearing in the technical grade of the active ingredient;

- (e) Require upper and lower certified limits of active ingredients, but only upper certified limits for inert ingredients;

- (f) Require certified limits for inert ingredients only when variations in the amount of the inert ingredient would affect the efficacy of the product or the hazard to man or the environment; or

- (g) Require certified limits for impurities only if they are present in quantities greater than 0.1 percent of the product.

Additional commenters stated that it was impossible to control the amount of ingredients within the narrow certified limits required by proposed § 163.61-6. They felt EPA should allow an applicant to set the certified limits at a broad range, such as three times the standard deviation from the mean value of the amount of impurity determined to be present in several batches of a product. Also, a broad range between upper and lower limits was considered particularly important when "overformulation" of rapidly-deteriorating active ingredients, like sodium hypochlorite, is necessary.

Responses - [The Agency refers the reader to part I.A. of the Discussion on Subdivision A for a more thorough explanation of legal authority.] As to legal authority, the Agency considers that it has the legal authority to require information which is necessary to carry out the purposes of the Act. Judged by that standard, EPA thinks that its requirements for certified limits are legal. EPA considers the requirement for certified limits not only to be

reasonable, but to be essential to its regulatory program. A "certified limit" is a statement of the maximum or minimum amount (usually expressed as a percentage of the product by weight) of an ingredient that will appear in a pesticide product. It is also a promise that any sample of the pesticide distributed in commerce will not exceed the maximum limits or fall below the minimum limits (if any) established for ingredients in the product. EPA intends to use this information when enforcing FIFRA sec. 12(a)(1)(C) which makes it unlawful to distribute a pesticide

> the composition of which differs at the time of its distribution or sale from its composition as described in the statement required in connection with its registration under Section 3.

Without "certified limits" or their equivalent, EPA would be unable to assure that the pesticides to which humans and the environment are actually exposed are safe. Hence, EPA believes that it is both reasonable and legal to require applicants to establish certified limits.

With regard to the suggestion that EPA must show a "specific need" for certified limits for "a given product" before it can require an applicant to establish limits, apparently the commenter anticipated that the Agency must demonstrate that a particular product contains an ingredient which would be hazardous, if the quantity of the ingredient were not regulated. This approach is totally inconsistent with the statutory scheme. To require EPA to make a finding about the risk of specific ingredients would, in effect, relieve applicants of the burden of proving that their pesticides were safe. The intent of Congress and the FIFRA which it enacted was to place this burden entirely upon applicants for registration.

As to the interpretation of ingredients which might be "reasonably identifiable" in proposed § 163.61-6, EPA agrees that this language was vague and would require applicants to establish certified limits for numerous ingredients which are unlikely to be present in a product in amounts that would be important for EPA to evaluate. The Agency recognizes, in addition, that a requirement to set a certified limit for each potential ingredient regardless of its quantity, such as for some of the minor ingredients in pine oil, could be quite burdensome, and probably would not provide particularly useful information to the Agency. Accordingly, the Agency has revised the requirements for certified limits. The universe of pesticide products was divided into two major groups for purposes of the requirements for certified limits. The first group consists of manufacturing-use products and those end-use products produced by an integrated formulation system. All other end-use products comprise the second group. Basically, a person seeking to register any kind of a pesticide product must establish an upper and lower certified limit for each active ingredient and each

intentionally-added inert ingredient. In addition, if the applicant's product is in the first group, an upper certified limit is required for each impurity associated with an active ingredient which was found (or theorized) to be present in quantities greater than 0.1 percent of the product by weight. [See § 62-2(b) and (c) in the current guidelines.] The reasons for this approach are explained below.

The Agency requires an upper certified limit for each active ingredient primarily to assess the upper bound of toxicity of the pesticide product. The Agency requires a lower certified limit for active ingredients for two reasons. First, the amount of an active ingredient in a product usually has a significant influence on the efficacy of a product. Thus, the Agency needs to know the lowest amount of the active ingredient that will be present in the pesticide product for which the producer believes the product will be efficacious.

The second reason for requiring a lower certified limit for active ingredients is that the Agency is concerned that a single pesticide product not have widely different toxicity based on differences in amount of active ingredient in the product. Large variations in the toxicity of different packages of a pesticide product would tend to undermine public confidence in the labeling of pesticide products. For example, assume that, when a product contained an amount of an active ingredient equal to the upper certified limit, it might cause severe skin burns, but when it contained an amount of active ingredient at the lower limit, it might be only mildly irritating to the skin. A warning appropriate for a package of the product containing the maximum amount of active ingredient would be inappropriate for a package of the product containing the minimum amount. A person who happened to purchase, use, and become exposed to the less dangerous product might thereafter ignore the warning when using other more dangerous packages of the product or when using different pesticide products with similar warnings. Thus, establishing the certified limits for an active ingredient assists the Agency in its review of precautionary label statements in relation to product content.

Upper and lower certified limits for intentionally-added inert ingredients are required for basically the same reasons. The presence of inert ingredients affects the toxicity, environmental fate, and efficacy of the product, and in order to evaluate these characteristics, the Agency needs to know how much of each intentionally-added inert ingredient will be present in a product.

Upper certified limits are required for impurities associated with an active ingredient and present in quantities greater than 0.1 percent of the product. Since impurities normally are not included to lower the toxicity or to alter the environmental fate or efficacy of the entire mixture, registrants would not need to assure the presence of a minimum amount of impurity in the product. Thus, only an upper certified limit

is required. EPA established the 0.1 percent cutoff on the assumption that impurities present in greater amounts are more likely to present risks to humans and the environment than impurities present in lesser amounts. Moreover, impurities which constitute at least 0.1 percent of the product will generally be easier to identify than those present in smaller amounts.

Finally, in addition to imposing a quantitative cutoff level below which routine analysis is not required for impurities, the Agency has limited the requirements for certified limits to those impurities associated with an active ingredient. [See the definition of this term in § 60-2(d).] The two reasons for treating those impurities differently from impurities associated with an intentionally-added inert ingredient have been discussed earlier in this Discussion under Part II.A.1. They are:

- Most impurities of concern are associated with the active ingredient; and

- Chemically-similar substances often produce similar biological effects.

For these reasons, the requirement for impurity certification extends only to those impurities associated with an active ingredient.

EPA has considered the several alternatives suggested by the different commenters. The requirement in the current guidelines is, generally, a combination of alternatives (d) and (g). Alternatives (a) and (c) were considered inadequate because they ignored the fact that ingredients which are not biologically active may nonetheless affect the toxicity, efficacy, or environmental behavior of other ingredients. In addition, alternative (a) is based on circular logic; EPA cannot tell whether an ingredient will be present in a toxicologically-significant amount (the criterion that would necessitate a certified limit) unless it knows how much of the ingredient is present (i.e., unless a certified limit has been established).

Alternative (b) suffers from the problems that would afflict reliance on any list. First, the list would change. Thus, current registrants who had provided product chemistry information when their products were initially registered would face the constant possibility that EPA would ask them to certify limits for substances newly added to the list. This would be burdensome for both registrants and EPA. Second, it would be difficult to assure that most ingredients which would be of concern to EPA were listed, since the potential risks of any ingredient depend not only upon its inherent toxicity but also on the presence or absence of other ingredients and on the amount of the ingredient in the product.

Alternative (e) not only fails to address impurities, but it would not require a lower certified limit for intentionally-added inert

ingredients. In other words, this suggestion assumes that the amount of any intentionally-added inert ingredient could vary from its upper limit (e.g., 90 percent of the product) to 0.0 percent. This variation would would make it exceedingly difficult to assess the toxicity and other characteristics of the product. Thus, the Agency needs lower limits for each intentionally-added inert ingredient. (See also the discussion at part II.G. of this Discussion.)

Alternative (f) ignores both active ingredients and impurities. More importantly, the Agency knows of virtually no intentionally-added inert ingredients (except some coloring and odor agents) that do not affect efficacy, toxicity, or environmental fate of a product. The Agency thinks a more sensible approach is to routinely require certified limits for all inert ingredients, and to handle exceptional cases by waivers.

Alternatives (d) and (g), together, correspond to the Agency's position in the current guidelines and to the requirement for certified limits which are specified by 40 CFR § 158.110. Note that the upper limit set for an impurity may include, when appropriate, structurally similar impurities. The Agency concludes that this section of the guidelines now requires applicants to submit only the information which is needed to evaluate the safety of their products, and does not impose unreasonable burdens.

D. Requirement for Analytical Methods.

Proposed § 163.61-7 would have required that the application for registration of a manufacturing-use product or an end-use product produced by an integrated formulation system contain certain analytical information. In particular, the application would have been required to contain an analytical method capable of measuring "each identifiable impurity that is present in the product in quantities of 0.01 percent (of the weight of the product) or more." A similar requirement would have been imposed on end-use products not produced by an integrated formulation system, except that the requirement extended only to impurities associated with the manufacture of the technical chemical. The following comments and responses concern these two requirements.

Comments - A number of commenters expressed major concerns about the requirement to analyze each manufacturing-use product for impurities present in quantities greater than 0.01 percent of the product. Their objections fell into three major categories. First, it is impossible to analyze products at such low levels. Second, even if such analysis were possible, EPA's requirements are completely unreasonable since they would do nothing to prevent unreasonable adverse effects on the environment. Finally, the cost of performing the required analysis is excessive in view of the small benefits which would result from having such information.

Some commenters described in detail the various procedures which are available for analyzing mixtures of different chemical substances. Descriptions of these procedures included discussion of the levels of sensitivity of such procedures, as well as the specific kinds of ingredients which could be detected using the procedures. With reference to these procedures, a number of registrants and other members of the public stated that current analytical methods are inadequate for analyzing complex mixtures like pesticide products with the level of sensitivity required by the proposed guidelines, and some stated flatly that such analyses are not reproducible. They noted that small changes in the manufacturing or formulating process could have a major impact on the number and level of impurities present at or near the 0.01 percent level. Commenters also noted that analysis to 0.01 percent would reveal many innocuous substances and might miss some important hazardous chemicals such as dioxins or nitrosamines that might be present in quantities less than 0.01 percent.

By far the majority of objections to the requirement for analysis at the 0.01 percent level were based on economic considerations. The commenters believed the proposal would impose extremely expensive requirements on people seeking to register pesticide products. Although the various cost estimates proffered by commenters varied significantly, all exceeded the costs estimated by the Agency's staff on economic impact of the proposal.

A wide range of alternatives to the requirement were suggested, including:

- (a) EPA should require applicants to retain samples of the products they produce and market. EPA could then demand that the applicant or registrant submit the samples for analysis whenever EPA desired information on the composition of pesticides actually being distributed in commerce.

- (b) EPA should require routine analysis only for ingredients present in a product at levels greater than 1.0 percent of the product.

- (c) EPA should require routine analysis of pesticides only for active ingredients present in quantities greater than 0.1 percent of the product.

- (d) Routine analysis should be required only for organic ingredients constituting more than 0.1 percent of a product.

- (e) EPA should require routine analysis to the 0.1 percent level for all ingredients.

- (f) EPA should require analysis of ingredients present at some level between 0.1 and 0.01 percent.

- (g) The requirements to analyze for ingredients present in quantities at or near 0.01 percent should be imposed only when the ingredient is known to cause toxicity problems.

- (h) EPA should require routine analysis for active ingredients, "major" inert ingredients, and other biologically-significant ingredients.

- (i) EPA should require analysis of the composition of pesticide products for ingredients which are expected to be "biologically active" or for ingredients which are demonstrated to be of concern.

- (j) EPA should require analysis of ingredients which have been identified as potentially significant by toxicity testing.

Responses - For many of the reasons stated in these comments, EPA revised its requirements concerning analytical methods. Basically, the final guidelines require that each applicant must submit a description of an analytical method capable of verifying the certified limits for the active ingredients and certain impurities (but not intentionally-added inert ingredients) in his pesticide product. (See § 62-3 of the current guidelines.) Since the requirements for analytical methods are based on the requirements for certified limits, it is useful to review those requirements. Every person who seeks to register a pesticide must certify upper and lower limits for all active ingredients and intentionally-added inert ingredients in a pesticide product. In addition, if the product is a manufacturing-use product or an end-use product produced by an integrated formulation system, the person must establish an upper certified limit for each impurity associated with an active ingredient which constitutes more than 0.1 percent of the product. (See § 62-2 of the current guidelines.) Thus, an analytical method is required for each active ingredient and, on a case-by-case basis, the impurities associated with an active ingredient that are present in quantities greater than 0.1 percent. Section 62-3 of the current guidelines contains a provision specifically waiving the requirement for an analytical method for any impurity which is on the Food and Drug Administration's GRAS (Generally Recognized As Safe) list or on EPA's list of ingredients exempt from the requirement for a tolerance (see 40 CFR 180.1001).

The current guidelines reflect a significant reduction in the requirements concerning analytical methods; such methods would not

be required for impurities present in quantities between 0.1 and 0.01 percent of a product. This change was recommended by numerous commenters, many of whom said that routine analysis to the 0.1 percent level was both feasible and reasonable. [See, generally, alternatives (c), (d), (e), and (f).]

The Agency has considered and rejected the other alternatives suggested. Alternative (a) is an unworkable approach because it fails to provide EPA with the information it needs to verify certified limits: a description of an analytical method. Moreover, there is a possible problem with limiting analysis only to samples which were retained by the producer; the sample might be highly unrepresentative of the product as distributed in commerce. The producer's samples, for instance, are unlikely to have been stored under the full range of conditions which might occur during commercial distribution of a pesticide, and thus they may have different amounts of degradation products compared to the commercially-marketed product.

EPA rejects alternative (b) because it would ignore a potentially significant group of impurities (those between 0.1 and 1.0 percent of a product), even though it would be comparatively inexpensive to obtain information about these substances. This alternative is also overly broad since it routinely includes intentionally-added inert ingredients.

Alternative (c) implicitly recognizes that analysis to 0.1 percent is feasible, but this alternative is unacceptable because it is limited to active ingredients. Active ingredients and their associated impurities are more likely to be hazardous than other substances in the product and, therefore, the Agency thinks it appropriate to require applicants to describe methods capable of identifying and measuring the the quantity of those substances.

Alternative (d), too, recognizes the reasonableness of a 0.1 percent cutoff, but it also is too restrictive in its scope. EPA thinks that some inorganic impurities (e.g., lead or mercury) can be as toxic as many organic impurities.

Of the suggestions received in public comments, alternative (e) is the closest to the Agency's current guidelines. This alternative, however, goes beyond the current guidelines by suggesting that applicants submit analytical methods for <u>all</u> ingredients, including, apparently, intentionally-added inert ingredients. These substances are relatively much less toxic, as a group, than active ingredients, and their amounts in pesticide products can be easily controlled in the manufacturing or formulating process. Moreover, developing analytical methods to detect and quantify

inert ingredients would be an extremely expensive effort, costing the pesticide industry billions of dollars. EPA believes that routinely requiring analytical methods for intentionally-added inert ingredients would not be worth the cost.

Alternative (f) suffers from the same problems as alternative (e), and raised the added difficulty that no specific cutoff level is defined.

Alternatives (g), (h), (i), and (j) all contain the idea that EPA should require an applicant to describe an analytical method only for those ingredients and impurities in a product which are potentially toxic to humans or "biologically active." The Agency sees merit in these suggestions. Eventually, EPA intends, as genotoxicity tests become more reliable, to require testing of all products (or, in some cases, all beginning materials used to formulate end-use products) in a battery of genotoxicity screening studies. Such studies are inexpensive, quick, sensitive, and moderately accurate predictors of the biological activity of chemical substances. Under these requirements, an applicant would be required to identify and quantify any product component which caused positive results in one-half of or more of the tests comprising the battery. While a positive test for such a battery would not be sufficient evidence to confirm a product component as a clear risk to humans, it would indicate whether a product contained a biologically-active component which the Agency should further evaluate.

Although other factors, such as the presence or absence of other ingredients, may affect the hazards posed by a product component, EPA needs to know its amount and its toxicity. Currently, EPA does not routinely obtain such information about ingredients other than for the active ingredients. Accordingly, it is difficult to develop any meaningful list of potentially-hazardous product impurities on the basis of the currently submitted data.

Currently, EPA only specifies criteria that will aid in identifying those product components and impurities which are likely to be of greatest concern. The requirement for certified limits reflect these criteria. The two criteria routinely used are:

(a) A component must be present in quantities equal to or greater than 0.1 percent; and

(b) An impurity must be associated with an active ingredient.

E. Accuracy and Precision of Methods.

Proposed § 163.61-7 required that analytical methods submitted for detecting and measuring product ingredients or impurities should include "qualitative confirmatory methods" and "validation data", and that the applicant "must supply his assessment of the sensitivity or limit of detection" in each of the methods.

Comments - A number of comments were received concerning the accuracy and precision of the analytical methods which would be used to satisfy the requirements of proposed § 163.61-7. The following statements reflect these comments:

- Less than 25 percent error of method may be difficult to obtain.

- An accuracy level of ± 25 percent and a precision level of ± 5 percent might be achieved for analysis of impurities present at the 0.01 percent level in most pesticides.

- Normal best practice analytical variation of ± 1 percent precludes defining the active ingredient content to better than ± 0.8 percent.

- An instrumental analysis, meticulously conducted, might characteristically yield a value for the major components that is within ± 0.5 percent of the true value.

- At the present time, a precision level of ± 0.05 percent is considered excellent.

Responses - EPA has added a new paragraph specifying the recommended relative standard deviation for analytical methods required by the guidelines. Section 62-3(b)(3)(iii) of the current guidelines provides:

> The Agency will evaluate the acceptability of an analytical method on the basis of the precision of the results obtained by the registration applicant on a homogeneous sample of the product. The following guide indicates the recommended levels of precision:

Ingredient measured in sample	Precision: 100 x (standard deviation ÷ arithmetic mean)
More than 10.0%	Not greater than 2%
1.0% up to 10.0%	Not greater than 5%
0.1% up to 1.0%	Not greater than 10%
Less than 0.1%	Not greater than 20%

F. Deferred Submittal of Data.

Proposed § 163.61-2(c) stated that data to meet the requirements of product chemistry be submitted at the time of registration, to the extent possible. However, for those data that could not be supplied at the time of registration, the data would have to be submitted within six months after commercial production had commenced. At the time of registration, a schedule would have to be submitted for those data that would be supplied later.

Comments - Many commenters misinterpreted this requirement, assuming that the late data would have to be submitted within six months after registration rather than six months after commercial production began. Commenters felt that these requirements should be revised to allow for more time before submittal. They supplied a number of reasons for allowing a registrant more than six months after registration to submit the required data. First, to the extent that data must be derived from testing a commercially-produced pesticide, they felt it was not possible to fulfill a data requirement until commercial production begins. They stated that a company will often not begin to build a commercial pesticide manufacturing plant until after EPA approves a registration. Construction could easily last longer than six months. Second, some products are only manufactured during certain times of the year (e.g., to meet seasonal demands) and that time might next occur more than six months after registration. Third, if the required data included determination of degradation products in the pesticide or development of analytical techniques for particular ingredients, the time needed to develop these data would last longer than six months, since both are time-consuming efforts. Last, the ingredients used in the process of manufacturing a pesticide change slightly during the year (e.g., seasonal variation in supply, adjustment of process to compensate for temperature differences). In order to obtain representative samples, a registrant may need to wait more than six months.

Because of the reasons discussed above, commenters recommended that EPA should modify the proposal concerning deferred submittal of data. The following alternatives were suggested:

- (a) Submittal within 12 months after registration.
- (b) Submittal "as soon as possible" or "as soon as practical" after registration.
- (c) Submittal "within a reasonable time, preferably six months after registration."
- (d) Submittal in accordance with a schedule determined on a case-by-case basis.

Responses - In spite of the fact that the basis for some of the comments was not sound, EPA has reconsidered the provisions of the proposal, and has removed the requirements for submitting data on the commercial product within six months after commercial production of the product. Instead, EPA has chosen to determine the schedule for submitting data based on testing with the commercially-produced pesticide on a case-by-case basis, using its authority under FIFRA sec. 3(c)(2)(B).

Alternative (a) is inappropriate for the same reasons as the original proposed 6-month requirement. Alternative (b) is unacceptable since it fails to establish a specific deadline for submitting the required data. Alternative (c) suffers from the combined difficulties of alternatives (a) and (b). Thus, EPA has chosen alternative (d) and will establish submission of the required data on a case-by-case basis.

G. Multiple Formulations.

It has long been the policy of the Agency to accept, under a single registration, multiple or alternate formulas for the same product. Typically, these alternate formulas show variation either in the percentage of composition or in trade names of inert ingredients such as surfactants, solvents, and similar product components. However, if directions for use or precautionary statements were different, separate registrations would be required. Obviously, if there were already separate registrations for variant formulas for a typical product, the registration applicant(s) would have been required to submit Product Chemistry data or information on each separate individual formula. Therefore, for the purposes of this Discussion, the Agency is proposing the same standard for multiple formulations under the same registration: each variant alternate formula beyond the basic formula would be subject to the applicable requirements in following sections of Subdivision D:

§ 60-3;
§§ 61-1 through -3;
§§ 62-1 through -3;
§§ 63-1 through -21;
§ 64-1.

SUBDIVISION D - GUIDELINES FOR PRODUCT CHEMISTRY

Series 60: GENERAL INFORMATION

§ 60-1 Overview

(a) Scope and purpose (1) This subdivision describes the data and other information concerning product chemistry which the Agency requires [see 40 CFR §§ 158.110 and 158.120] in support of registration of pesticide products. Product chemistry data and information are used by the Agency primarily to establish the composition of each pesticide product; basic information which is needed to assess toxicity to humans and hazards to the environment resulting from use of the product. Product composition is reported in the Confidential Statement of Formula which identifies and gives the amounts of the active ingredients, intentionally-added inert ingredients and, in some cases, the impurities contained in each product. Product chemistry data and information are also needed to assess the physical and chemical hazards of products, such as corrosiveness, explosiveness, and flammability.

(2) Each applicant submits data which explain and support the information reported in the Confidential Statement of Formula submitted for each product. These data include information on the beginning materials used in manufacture of the product, a description of the manufacturing process, a theoretical discussion of the formation of impurities, the results of analysis of manufacturing-use products and integrated formulation system products, and assurance through certified limits that the composition will not vary from that described at registration. The Agency also requires an analytical methodology appropriate for use in verifying certified limits for the active ingredients and certain other ingredients. Registrants of most end-use products can obtain analytical methods from the basic manufacturer of the active ingredient.

(3) Information on a number of physical and chemical properties is required to characterize active ingredients in their technical or purer form, and to characterize manufacturing-use products and end-use products. Determination of other physical and chemical properties is required to assess hazards posed by products to man and the environment and to determine appropriate labeling cautions for such products.

(b) List of requirements. The Product Chemistry data requirements can be found in 40 CFR Part 158. The guidelines

sections describing the information and data required for manufacturing-use and end-use formulated products are as follows:

Product identity	§ 61-1(a)
Confidential Statement of Formula and information on ingredients	§ 61-1(b)
Manufacturing process	§ 61-2
Discussion of the formation of impurities	§ 61-3
Preliminary Analysis of product samples	§ 62-1
Certification of ingredient limits	§ 62-2
Analytical methods for certified limits	§ 62-3
Physical and chemical characteristics	§§ 63-1 through -21
Submittal of samples	§ 64-1

(c) Application status and compliance. The requirements imposed by 40 CFR Part 158 apply to products already registered as well as those being proposed for registration.

(1) When supporting data are not adequate the Agency will notify registrants of products already registered, either (occasionally) through the data call-in program, or (routinely) upon development of a registration standard as to what additional product chemistry data must be submitted. Current product registrations will remain valid so long as registrants comply with the terms of the subsequent Agency notification.

(2) For purposes of conditionally registering a new product under FIFRA section 3(c)(7)(A) or (B) ("Me-Too" registration or registration of additional uses) applicants must submit the product chemistry data and information required by 40 CFR § 162.18-2(c)(1) or (d)(1). These requirements and those for conditional registrations under FIFRA section 3(c)(7)(c) (Experimental-use permits) are listed in more detail in 40 CFR § 158.120. These data requirements (which are quoted below) correspond to the following sections of the product chemistry guidelines:

Conditional registration - Product chemistry data requirements	Corresponding section(s) of product chemistry guidelines
I. Manufacturing-use Products	
§ 162.18-2 (c)(1)(i): "Product identity and disclosure of ingredients, including impurities"	§ 61-1, Product Identity and Disclosure of Ingredients
(c)(1)(ii): "A description of the manufacturing process, including composition and purity of starting and intermediate materials"	§ 61-2, Description of Beginning Materials and Manufacturing Process

(c)(1)(iii): "Analytical methods and sample assays for the impurities"	§ 62-1, Preliminary Analysis of Product Samples
(c)(1)(iv): "Physical and chemical properties"	§§ 63-1 and 63-2 through 63-13 (part of) Physical and Chemical Characteristics
(c)(1)(v): "If requested by the Agency, a sample of the technical product"	§ 64-1, Submittal of Samples

II. End-use Products

§ 162.18-2 (d)(1)(i): "Product identity and disclosure of ingredients"	§ 61-1, Product Identity and Disclosure of Ingredients
(d)(1)(ii): "If requested by the Agency, a sample of the product proposed for registration"	§ 64-1, Submittal of Samples
(d)(1)(iii): "If any active ingredient of the formulated (end-use) product is derived from any substance other than a registered product, data required by paragraph (c) of this section"	§§ 61-1, -2; 62-1; 63-1 through -21; and 64-1 (see items above for titles)

Prior to granting a conditional registration, the Agency may, on a case-by-case basis, require additional product chemistry data or information. In addition, applicants for conditional registration under FIFRA sec. 3(c)(7)(A) or (B) must satisfy the other data requirements in this subdivision by the same date as that set for similar products already registered.

(3) The product chemistry data requirements for applicants for conditional registration under FIFRA sec. 3(c)(7)(C) will be determined on a case-by-case basis.

(4) For products being proposed for full registration under FIFRA sec. 3(c)(5), applicants must satisfy all of the data requirements of 40 CFR Part 158 prior to full registration.

§ 60-2 Definitions.

Terms used in this subdivision shall have the meanings set forth in sec. 2 of FIFRA, in 40 CFR § 162.3, and in 40 CFR Part 158. In addition:

(a) The term "beginning material" means any substance which constitutes or contains any of the product's active or intentionally-added inert ingredients or which constitutes or contains a chemical precursor of any ingredient used in making the product.

(b) The term "end-use product" means a pesticide product intended to be labeled with instructions for direct use or application for pesticidal purposes.

(c) The term "impurity" means any substance in a pesticide product other than an active ingredient or an intentionally-added inert ingredient; the term includes beginning materials, side-reaction products, contaminants, and degradation products.

(d) The term "impurity associated with an active ingredient" means:

(1) Any impurity present in the technical grade of the active ingredient (e.g., a substance carried over from a beginning material, or from an intermediate, and impurities formed through side-reactions or by degradation of the active ingredient); and

(2) Those impurities which form in a pesticide product through reactions between the active ingredient and other substances in the product, or in the packaging of the product.

(e) The term "integrated formulation system" means a process for producing an end-use product through the use of any substance which contains an active ingredient and which:

(1) Is not a registered manufacturing-use product; or

(2) Was produced or acquired in a manner that does not permit its inspection by the Administrator under sec. 9(a) of FIFRA, prior to its use in the process.

(f) The term "intentionally-added inert ingredient" means any ingredient of a product (other than an active ingredient) which is intentionally made a part of the product to serve some useful function.

(g) The term "manufacturing-use product" means any pesticide product other than an end-use product. Usually, these products contain only the technical grade of the active ingredient or a high

concentration of the active ingredient with small amounts of inert ingredients such as stabilizers and similar substances.

(h) The term "nominal concentration" means the amount of an ingredient which is expected to be present in a typical sample of a pesticide product.

(i) The term "technical grade of an active ingredient" (which is synonymous with the term "technical chemical") means a material:

(1) Which contains an active ingredient;

(2) Which is produced on a commercial or pilot-plant scale (though it may never be held for sale); and

(3) To which no ingredient has been deliberately added for any purpose other than synthesis or purification of the active ingredient.

§ 60-3 General provisions.

(a) Data on the pesticide product. Except as noted by paragraph (c) of this section, the data and information described in §§ 61-1 through 64-1 shall be based on the product as commercially produced. Thus, for example, data specified by §§ 63-1 through -21 (physical and chemical characteristics) must be derived from studies conducted with a test substance representative of the commercial product, and the information specified by § 61-2 (Description of beginning materials and manufacturing process) must describe the commercial production process.

(b) Omitting certain of the required data. (1) Some of the information specified by §§ 61-1 through 63-21 might prove to be extremely difficult to develop, especially with respect to certain highly complex organic or inorganic substances (e.g., corn cobs, clay, and synthetic polymers). In some cases the applicant may know of no way even to attempt to develop such data, and in other cases he may find that one or more plausible means to develop the data are in fact incapable of producing the data. In either case, the applicant may omit such data, but he shall describe all attempts made to obtain the information or data. If some appropriate means to meet the requirement has not been undertaken, the Agency will specify for the applicant what additional efforts must be undertaken. If these efforts are not undertaken, the Agency may refuse to register the product.

(2) Applicants may omit data and information on grounds other than those specified in paragraph (b)(1) of this section. The Agency will consider these requests on a case-by-case basis.

(c) Timing of data submissions. Except as provided in paragraphs (c)(1), (2), and (3) of this section, each applicant for registration of a new product shall supply the data and information required by 40 CFR Part 158 at the time the application for registration is made. For products already registered, registrants shall submit the required data at the time indicated in a notice issued pursuant to FIFRA sec. 3(c)(2)(B). See also § 60-1(c).

(1) Deferral of data submission for products not in commercial production. Some applicants may consider it impractical to construct facilities to produce their products in commercial quantities prior to receiving registration for their products. Thus, they may not be able to provide data, as required by this subdivision, from studies which use a test substance representative of the commercially-produced product. Upon request, the Agency will consider deferring the requirement to submit such data until after the registration of the product is approved. (Note: a decision to allow deferment of data does not necessarily mean that the Agency will approve the registration of the product for which deferred submission of the data is allowed.)

(2) Contents of a deferral request. A request for deferral must contain:

(i) A statement that the applicant has no facilities for producing the product in commercial quantities and does not intend to construct such facilities until the product is registered;

(ii) Based on material produced on a pilot scale, the data required by 40 CFR §§ 158.110 and 158.120.

(iii) A description of the commercial manufacturing process (see § 61-2), a discussion of the formation of impurities in the commercially-produced product (see § 61-3), and a discussion of changes in the certified limits for the product which might result from differences between the pilot-scale and commercial production processes; and

(iv) A schedule for submitting the other data required by 40 CFR Part 158 based on the commercially-produced material.

(3) Notification for submittal of deferred data. If the Agency approves a request for deferred submission of data on commercially-produced material, and if the product is otherwise acceptable for registration, the product will be registered and the registrant at the same time will be furnished a notice under FIFRA sec. 3(c)(2)(B) requiring submission of the deferred data as soon as possible after the commercial production facilities are completed.

(d) Confidential treatment of product chemistry information. Information submitted by applicants or registrants concerning product chemistry will be afforded confidential treatment only to the extent required by FIFRA sec. 10. A person submitting information entitled to confidential treatment under sec. 10 should comply with the procedures in 40 CFR § 2.203.

Series 61: PRODUCT IDENTITY AND COMPOSITION

§ 61-1 Product identity and disclosure of ingredients.

In accordance with 40 CFR § 158.120, each product's registration must be supported by the following:

(a) Information on product identity. This information includes:

(1) The product name;

(2) The trade name(s) (if different); and

(3) The company code number(s) (optional).

(b) Statement of Formula. Each product's registration shall be supported by a statement describing the product's composition. A request for an amended registration other than for amending the statement of composition may state that an accurate and current description of the product's composition is already on file with the Agency's Registration Division, if that is the case. The statement of composition should contain:

(1) The name, nominal concentration, and certified limits for each active ingredient and each intentionally-added inert ingredient; and

(2) The name and upper certified limit for each impurity or each group of impurities for which a certified limit is required (see § 62-2);

(3) The purpose of each active ingredient and each intentionally-added inert ingredient;

(4) For each ingredient required to be listed by paragraph (b)(1) of this section, the chemical name from the Chemical Abstracts Index of Nomenclature or other well-defined name, and the Chemical Abstracts Service (CAS) Registry Number; and

(5) For each active ingredient: the product name, trade name, and common name (if established); the molecular, structural, and

empirical formulas; the molecular weight or weight range; and any experimental or internal code number the company has assigned.

§ 61-2 Description of beginning materials and manufacturing process.

(a) Beginning materials. Each product's registration must be supported by the following information on each beginning material:

(1) If the beginning material is a registered manufacturing-use pesticide product, the registration number of the product.

(2) For each other beginning material:

(i) The name and address of the manufacturer or producer of the beginning material or, if that information is not known by the applicant, the name and address of the supplier of the beginning material;

(ii) Each brand name, trade name, or similar commercial designation of the beginning material used by the manufacturer, producer, or supplier of the beginning material;

(iii) A copy of all available technical specifications, data sheets, and other documents by which the manufacturer, producer, or supplier of the beginning material describes its composition, properties, or toxicity; and

(iv) All other information which the pesticide product's producer has concerning the qualitative and quantitative composition of the beginning material.

(b) Manufacturing process. Each product's registration must be supported by an accurate and current description of the process used to manufacture or formulate the product. The description will normally contain the following information:

(1) A statement of whether the process is a batch or continuous process;

(2) The relative amounts of beginning materials and the order in which they are added;

(3) A description of the equipment used to produce the product which may influence the product's composition;

(4) A description of the physical conditions (e.g, temperature, pressure, humidity) which are controlled during each step of the process in order to influence the product's composition, and the parameters that are maintained;

(5) A statement of whether the process for producing the product involves intended chemical reactions (that is, combination of beginning materials which are expected to react with each other to produce an active ingredient or intentionally-added inert ingredient);

(6) A flow chart with chemical equations of each intended chemical reaction occurring at each step of the process;

(7) The duration of each step of the process;

(8) A description of any purification procedures, including procedures to recover or recycle starting materials, intermediates, or the final product; and

(9) A description of measures taken to assure the quality of the final product, including procedures involving the equipment used for blending product components and for filling and packaging.

(c) Changes in beginning materials or manufacturing process. Under FIFRA sec. 6(a)(2) registrants are required to inform the Agency of changes made in beginning materials or in the manufacturing process when such change alters substantially the product's composition; other changes need not be reported. In such instances, if the change effects the certified limits established in accordance with § 62-2, the provisions of § 62-2(a)(7) apply (i.e., a revised statement of certified limits must be submitted). Note that formulators are also expected to provide current information on the identity of their suppliers.

§ 61-3 Discussion of the formation of impurities.

(a) General requirements. In accordance with 40 CFR § 158.120 each product's registration must also be supported by a discussion of the impurities that may be present in the product, and why they may be present. The discussion should be based on established chemical theory and the information submitted under § 61-2 concerning the beginning materials and manufacturing processes used to make the product. The types of impurities which must be discussed are specified in paragraphs (b) and (c) of this section.

(b) Manufacturing-use products and those end-use products produced by an integrated formulation system. In the discussion referred to by paragraph (a) of this section, an applicant for registration of a manufacturing-use product or of an end-use product produced by an integrated formuulation system should discuss:

(1) Each impurity which he believes may be present in his product as marketed at a level equal to or greater than 0.1% (1000 ppm), based on his knowledge of:

(i) The composition (or composition range) of each beginning material which he uses to produce any active ingredient of his product;

(ii) The composition (or composition range) of each beginning material containing an active ingredient which he purchases (or otherwise obtains from another) and uses to produce his product;

(iii) The composition (or composition range) of each intentionally-added inert ingredient of his product;

(iv) The impurities which he knows are present, or believes are likely to be present, in the materials mentioned in paragraphs (b)(1)(i), (ii), and (iii) of this section, and the known or presumed level (or range of levels) of those impurities;

(v) The substances which result from the intended (main) reactions and side reactions which occur in the manufacturing and formulation of his product, and the relative amount of each such substance produced;

(vi) Degradation of any of the product's active ingredients after production of the product but prior to its use, and post-production reactions between any of the product's active ingredients or intentionally-added inert ingredients and any other components of the product or its packaging;

(vii) Migration of components of packaging materials into the product;

(viii) Contaminants resulting from earlier use of production equipment to produce other products or substances; and

(ix) The process control, purification, and quality control measures he uses; and

(2) Each other impurity which was found to be present in any analysis of the product he has conducted.

(c) End-use products not produced by an integrated formulation system. (1) In the discussion required by paragraph (a) of this section, an applicant for registration of an end-use product which is not produced by an integrated formulation system should discuss each impurity which may be present in his product as marketed at a level equal to or greater than 0.1 percent (1000 ppm), based on his knowledge of:

(i) The carry-over of impurities present in any registered product which serves as the source of any of his product's active ingredients. (As explained in preamble, the "formulators' exemption"

[see also the FIFRR Sec. 3(c)(2)(D)] applies to the requirement to develop quantitative data concerning the impurities present in registered products.)

(ii) The carry-over of impurities present in the intentionally-added inert ingredients of his product;

(iii) Reactions occurring during the production of his product between any of the product's active ingredients, between the active ingredients and intentionally-added inert ingredients, or between the active ingredients and the production equipment;

(iv) Post-production reactions between any of the product's active ingredients and any other component of the product or its packaging;

(v) Migration of packaging materials into the product;

(vi) Contaminants resulting from earlier use of production equipment to produce other products or substances.

(2) On a case-by-case basis, the Agency may require further discussion of possible chemical reactions involving other ingredients.

Series 62: ANALYSIS AND CERTIFICATION OF PRODUCT INGREDIENTS

§ 62-1 Preliminary analysis of product samples.

(a) When required. In accordance with 40 CFR § 158.120, composition data based on a preliminary analysis of the product will be required to support the registration of each manufacturing-use product and those end-use products produced by an integrated formulation system. If the technical chemical has not been used as a formulating ingredient in registered products, the preliminary analysis will include analyses of both the product and the technical chemical (TGAI). In the analysis of such technical chemicals the degree of accountability (or closure) is to be indicated (and typically $\geq$ ca 98%). Preliminary analysis of end-use products not produced by an integrated formulation system will be required only on a case-by-case basis.

(b) Requirements for performing sample analyses. (1) Selection of samples. (i) Five or more representative samples should be selected for the preliminary analysis.

(ii) If the product is produced by a batch process, each sample should be taken from a different batch of the product.

(iii) If the product is produced by a continuous process, samples should be taken at intervals sufficiently spaced to provide representative aliquots.

(iv) On a case-by-case basis, the Agency may require the analysis of additional samples.

(2) What ingredients to look for. If the product is a manufacturing-use product or an end-use product produced by an integrated formulation system, each sample should be analyzed for each of the following ingredients:

(i) Each active ingredient; and

(ii) Each impurity for which a certified limit is required. [See § 62-2(b)(2).]

(3) Selection of analytical methods. For the analyses indicated by paragraph (b)(2) of this section, the applicant may use any appropriate analytical methods.

(4) Additional requirements. On a case-by-case basis, the Agency may require the analysis of samples for additional ingredients, including intentionally-added inert ingredients, or analysis using more sensitive or more accurate analytical methods.

(c) Description of analytical methods and reporting of sample analysis results. (1) Description of analytical methods. The report on the results of analysis of product samples indicated by this section should contain a description of (or reference to) each analytical method used to detect the presence of, or to quantify the amount of, each ingredient in each sample. The description of each method should include:

(i) A complete, detailed description of each step in the analytical method; and

(ii) A statement of the precision and accuracy of the analytical method.

(2) Reporting of sample analysis results. The report on the results of analysis of product samples indicated by this section should contain the results from each analysis conducted on each sample.

(i) The results should include the identity of each ingredient for which the analysis was conducted, the quantity (if any) detected, and the mean and relative standard deviation of reported analytical results.

(ii) The results should be reported to at least the first decimal place (e.g., 97.1%, 2.4%); or if the measured quantity of an active ingredient is less than 1.0%, the results should be reported to the first significant figure (e.g., 0.9%, 0.05%, 0.001%).

(d) Identifying spectral data. If requested by the Agency, identifying spectral data shall be submitted for the product or any substance listed in its statement of composition. The spectral data which may be requested include infrared, nuclear magnetic resonance, ultraviolet, and mass spectra.

(e) References. For guidance in conducting the analysis of samples as requested by this section, the applicant is referred to the following publications:

(1) Bontoyan, W.R., ed. 1976. Manual of chemical methods for pesticides and devices. U.S. Environmental Protection Agency. Published and distributed by the Association of Official Analytical Chemists, Arlington, Virginia.

(2) Horwitz, W., ed. 1980. Official Methods of Analysis of the Association of Official Analytical Chemists. Association of Official Analytical Chemists, Arlington, Virginia.

(3) CIPAC Handbook, Vol. 1. (1970) and Vol. 1A. 1980. Collaborative Handbook. International Pesticides Analytical Council Limited, Plant Pathology Laboratory, Hatching Green, Harpenden, Hertfordshire, England.

(4) Zweig, G., and J. Sherma, eds. 1963-1978. Analytical methods for pesticides and plant growth regulators. Continuing series. Academic Press, New York, N.Y.

§ 62-2 Certification of ingredient limits.

(a) General. (1) Requirement and considerations. (i) In accordance with 40 CFR § 158.110, each registration must be supported by a certification that each upper and lower limit established in accordance with paragraph (b), (c), or (d) of this section will be maintained for all quantities of the product sold or distributed in commerce. Certified limits are used in two ways. First, the Agency will consider the certified limits in making the registration determination required by secs. 3(c)(5), 3(c)(7), and 3(d) of the

Act and in making other regulatory decisions required by the Act. Second, the Agency will collect and analyze commercial samples of the registered products. When, upon analysis, the composition of such samples is found to differ from that certified, the results may be used by the Agency in regulatory actions under sec. 12(a)(1)(C) and other pertinent sections of FIFRA. [See paragraph (a)(6) of this section.]

(ii) In certifying a limit for a rapidly degrading ingredient, the applicant or registrant should consider carefully the maximum quantity needed to assure the declared strength of the product for its stated life. [See paragraph (a)(5) of this section.] The applicant should note the possibility that increasing the amount of active ingredient in a product may place the product in a higher category of toxicity or result in residues exceeding an established tolerance.

(2) Submittal of explanations. The applicant or registrant should submit an explanation of how each certified limit was established (e.g., by sample analysis, quantitative estimate based on amounts of ingredients used, etc.) and what is known about the accuracy and precision of the procedures used to establish the limit.

(3) Expression of limits. The limits certified for ingredients should be stated as percentages of the total product, calculated by weight.

(i) For each ingredient present in quantities equal to or greater than 1.0 percent, limits should be expressed to the first decimal place.

(ii) For each ingredient which may be present in quantities less than 1.0 percent, limits should be expressed to the first significant figure.

(4) Setting appropriate certified limits. The Agency suggests that the range between the upper and lower certified limit for each active ingredient and each intentionally-added inert ingredient be based on a consideration of the variability of each of these ingredients when normal quality assurance procedures are utilized in the production process. To be acceptable for the purposes specified in § 158.22 (a), the limits stated for each intentional ingredient should not greatly exceed its actual variability in the product.

Unless a lower level is specifically requested by the Agency, the applicant is expected to set upper levels for impurities at levels exceeding levels normal to the product by a reasonable amount and which would not be expensive or difficult for a manufacturer to certify.

(5) Duration of limits. The certified limits become effective upon Agency approval in connection with registration of the product, and would apply to all units of the product in channels of trade until the expiration date specified on the product label or, if no such date is specified, for as long as the product is available for sale.

(6) Enforcement of limits. The Agency may use the analytical methods submitted under § 62-3 or any other scientifically-sound method to determine whether the composition of a product conforms to the limits certified under this section. If the Agency determines that the amount of an ingredient in a product does not fall within the certified limits, the Agency will regard the product to be in violation of FIFRA sec. 12(a)(1)(C) or other pertinent sections of the Act and subject to possible regulatory action. However, if such a determination is based upon improved methodology and the violation occurred because both methods submitted under § 62-3 and data submitted under § 62-1 were definitely erroneous, the registrant shall not be subject to regulatory action provided he makes the necessary corrections in his product within a reasonable time, which will be specified by the Agency.

(7) Revision of limits. If a registrant desires to amend the certified limits for his product, he may apply for an amendment to the registration. Until the amendment has been accepted by the Agency in connection with registration of the product, the currently approved limits will apply to the product.

(b) Manufacturing-use products and those end-use products produced by an integrated formulation system. The statement of formula for a manufacturing-use product or for an end-use product produced by an integrated formulation system [see § 61-1(b)] shall contain, as required by 40 CFR § 158.110, the following certified limits:

(1) For each active ingredient and each intentionally-added inert ingredient, an upper and lower limit;

(2) For each impurity (or, if appropriate, for each group of structurally-similar impurities) associated with an active ingredient that was indicated in the discussion required by § 158.24 as being potentially present at a level equal to or greater than 0.1% by weight, an upper limit; and

(3) For each other impurity (or, if appropriate, for each group of structurally-similar impurities) associated with an active ingredient that was found in any sample in quantities equal to or greater than 0.1 percent by weight, an upper limit.

(c) End-use products not produced by an integrated formulation system. The statement of formula for an end-use product not produced by an integrated formulation system [see § 61-1(b)] shall contain, as required by 40 CFR § 158.110, upper and lower certified limits for each active ingredient and each intentionally-added inert ingredient.

(d) Certified limits for additional ingredients and impurities. The Agency may require, on a case-by-case basis:

(1) More precise limits;

(2) Certified limits for additional ingredients;

(3) More thorough explanation of how the certified limits were determined;

(4) Certified upper limits for impurities which will be present at levels lower than 0.1 percent (1,000 ppm) of the product; or

(5) A narrower range between the upper and lower certified limits than that proposed by the applicant.

§ 62-3 Analytical methods to verify certified limits.

(a) When required. In accordance with 40 CFR § 158.120, analytical methods to verify certified limits, as specified by paragraphs (b) and (c) of this section, are required to support the registration of each manufacturing-use product and each end-use product.

(b) Requirements for analytical methods and supporting data. (1) Substances for which methods are required. (i) If the applicant's product is a manufacturing-use product or an end-use product produced by an integrated formulation system, an analytical method is required for:

(A) Each active ingredient; and

(B) Each impurity for which a certified limit is required (see § 62-2) unless it is exempt from the requirement to obtain a tolerance and complies with the provisions of 40 CFR 180.1001, or it is a substance designated by the Food and Drug Administration as generally recognized as safe (GRAS) when it is a component of food. (See 21 CFR 182, 184, and 186.)

(ii) If the applicant's product is an end-use product not produced by an integrated formulation system, an analytical method meeting the requirements of paragraph (b)(3) of this section is required for each active ingredient.

(iii) On a case-by-case basis, the Agency may require analytical methods for additional ingredients.

(2) Analytical methods and supporting data for impurities. For most product impurities, the analytical methodology and data provided by the preliminay analysis [see § 62-1 (c)(1)(i) and (ii)] are expected to be sufficient. However, in some instances, the Agency may require the applicant to develop better, more precise methodology and provide more quantitative data. In making such a decision, the Agency will consider the toxicological and environmental significance of the impurity.

(3) Precision and accuracy of analytical methods. (i) For active ingredients (and for those intentionally-added inert ingredients for which the Agency may require methodology), the method must have sufficient precision and accuracy to determine whether the amount of such an ingredient found in any sample of the product is within the limits certified for that ingredient.

(ii) If an analytical method for an impurity is required, the method must have sufficient precision and accuracy to determine whether the amount of such impurity found in any sample of the product exceeds the upper limit certified for the impurity.

(iii) The Agency will evaluate the acceptability of an analytical method for an active ingredient or an intentionally-added inert ingredient (if methodology for the inert is specifically required by the Agency) on the basis of the precision of the results obtained by the applicant on a homogeneous sample of the product. The following guide indicates the recommended levels of precision:

Ingredient measured in sample	Precision: 100 x (standard deviation ÷ arithmetic mean)
More than 10.0%	Not greater than 2%
1.0% up to 10.0%	Not greater than 5%
0.1% up to 1.0%	Not greater than 10%
Less than 0.1%	Not greater than 20%

(iv) The analytical methods required by this section should be as simple, quick, and inexpensive to perform as possible, while satisfying the requirements of paragraphs (b)(3)(i), (ii), and (iii) of this section.

(4) Validation studies. Each analytical method shall be validated by studies of the precision and accuracy of the method (including, when appropriate, qualitative confirmatory methods).

(c) Description of analytical methods. (1) Each analytical method required by this section shall be described fully. The description shall identify each step of the analytical method and provide sufficient information for an analytical chemist to perform the analysis properly. If the method has been reported in the scientific literature or previously submitted to the Agency in support of the registration of another product, the applicant may submit an appropriate reference to the method. In such cases, a reprint or copy of the method should be included with the submission to help expedite Agency review.

(2) Validation data shall be provided for each analytical method required by this section. The applicant shall indicate the level of precision and accuracy of each method, as demonstrated by the validation data.

Series 63: PHYSICAL AND CHEMICAL CHARACTERISTICS

§ 63-1 General provisions for physical and chemical characteristics testing.

(a) Summary of test requirements. (1) Table 1 lists the chemical and physical properties for which tests are required by 40 CFR § 158.120. The table also indicates the kind of test substance that must be used in each test. The reader should consult each individual section for details, as the table only summarizes some of the basic test requirements.

(2) The "formulators' exemption" contained in FIFRA sec. 3(c)(2)(D) applies to the data requirements of §§ 63-2 through -13 of this subdivision. This exemption provides that an applicant for registration of an end-use product who purchases and legally uses a registered product to formulate his end-use product is not required to submit or cite any data under this subdivision pertaining to the safety of such purchased product. However, the purchased product must be registered and labeled for manufacturing-use or, if is an end-use product, it must be reformulated by the applicant for the same use as the purchased product.

(b) Test methods and the "References" paragraphs. (1) Most of the following sections, §§ 63-2 through -21, contain a paragraph entitled "Reference" or "References." These paragraphs list references to various published testing methodologies appropriate for making the required determinations. Unless specifically stated otherwise, the Agency recommends (but does not require) use of the referenced methodologies. Applicants may use any other scientifical

ly-sound techniques, provided that data are presented to show that the techniques used produce results comparable to the referenced methodology.

(2) References that denote "ASTM" refer to standardized methods published by the American Society for Testing and Materials, Philadelphia, Pa. References denoting "CIPAC" refer to standardized methods of the Collaborative International Pesticides Analytical Council, Ltd., Hatching Green, Harpenden, Hertfordshire, England.

(c) General reporting requirements. (1) Any methods used to meet the requirements discussed in §§ 63-2 through -21 shall be referenced or described in the application for registration. If methods used are listed in the references paragraphs of this section series, reference to the methods will suffice. If other methods are used, references may be used only if the instructions are readily available in texts or periodicals; otherwise, copies of such methods must be submitted with the application.

(2) The applicant shall submit his own statistical evaluations of the precision of these measurements (e.g., standard deviations or confidence intervals) when appropriate.

(d) General references. The Agency considers the following publications to contain useful information and acceptable procedures for conducting the tests required by this section:

(1) Weissberger, A., ed. 1959-1970. Technique of Organic Chemistry. InterScience Publishers, New York, N.Y.

(2) American Society for Testing and Materials. (Continuing series) Annual Book of ASTM Standards. Amer. Soc. for Testing and Materials, 1916 Race St., Phila., Pa. 19103.

(3) Environmental Protection Agency. 1976. Guidelines for registering pesticides in the United States. Fed. Reg. 40(123): 26802-26927. (June 25, 1975).

(4) Environmental Protection Agency. 1979. Toxic Substances Control - Discussion of premanufacture testing policy and technical issues; Request for comment. Fed. Reg. 44(53): 16240-16292. (March 16, 1979).

(5) CIPAC Handbook. Vol. 1. (1970), and CIPAC Handbook. Vol. 1A (1980), Collaborative International Pesticides Analytical Council, Ltd., Plant Pathology Lab., Hatching Green, Harpenden, Hertfordshire, England.

TABLE 1. PHYSICAL AND CHEMICAL PROPERTIES TEST REQUIREMENTS

FROM 40 CFR § 158.120

Section and title	Test substance		
	Technical grade of active ingredient	Manufacturing-use product	End-use product
63-2 Color	yes	yes	yes
63-3 Physical state	yes	yes	yes
63-4 Odor	yes	yes	yes
63-5 Melting point	yes (solids)	no	no
63-6 Boiling point	yes (liquids)	no	no
63-7 Density, bulk density, or specific gravity	yes	yes	yes
63-8 Solubility	yes	no	no
63-9 Vapor pressure	yes (pure form)	no	no
63-10 Dissociation constant	case-by-case (pure form)	no	no
63-11 Octanol/water partition coefficient	yes, for non-polar organics (pure form)	no	no
63-12 pH	yes	yes	yes
63-13 Stability	yes	no	no
63-14 Oxidizing or reducing	no	yes	yes
63-15 Flammability - flashpoint:	no	yes (combustible liquids only)	yes
- flame extension:	no	no	yes (aerosols only)
63-16 Explodability	no	yes	yes
63-17 Storage stability	no	yes	yes
63-18 Viscosity	no	yes (liquids only)	yes
63-19 Miscibility	no	yes (emulsifiable liquids only)	yes
63-20 Corrosion characteristics	no	yes (when packaged in metal, plastic, or paper containers)	yes
63-21 Dielectric breakdown voltage	no	no	yes (If for use around electrical equipment)

§ 63-2 Color.

(a) When required. (1) End-use products. A statement of the color of the end-use product and of the technical grade of each active ingredient in the product is required by 40 CFR § 158.20 to support the registration of each end-use product.

(b) Manufacturing-use products. A statement of the color of the manufacturing-use product and of the technial grade of each active ingredient in the product is required by 40 CFR § 158.120 to support the registration of each end-use product.

(c) Reporting. A description of the color (or lack of it) of each substance shall be reported. Any intentional coloration or discoloration, in accordance with the FIFRA sec. 3 regulations (see 40 CFR § 162.13) shall be reported in terms of the Munsell color system, together with the name of the coloring or discoloring agent and the percentage by weight of the product for such agent. The applicant is referred to paragraph (d) of this section for the source of information on the Munsell color system.

(d) References.

(1) ASTM D1535-68.

(2) Information on the Munsell color system may be obtained from Munsell Color, MacBeth Color and Photometry, Div. of Kollmorgen Corp., 2441 N. Calvert St., Baltimore, MD 21218.

§ 63-3 Physical state.

(a) When required. (1) End-use products. A description of the physical state of the end-use product and the technical grade of each active ingredient in the product is required by 40 CFR § 158.120 to support the registration of an end-use product.

(2) Manufacturing-use products. A description of the physical state of the manufacturing-use product and the technical grade of each active ingredient in the product is required to support the registration of a manufacturing-use product.

(b) Test method. The description of the physical state of each substance shall be based on a visual inspection of the substance at 20°C or 25°C.

(c) Reporting. Conventional terms such as "solid," "granular," "semisolid," "mixture of liquid and solid," "volatile liquid," "powder," "gas," and similar terms shall be used, as appropriate, to describe each substance.

§ 63-4 Odor.

(a) When required. (1) End-use products. A description of the odor (or lack of it) of each end-use product and the technical grade of each active ingredient in the product is required by 40 CFR § 158.120 to support the registration of an end-use product.

(2) Manufacturing-use products. A description of the odor (or lack of it) of the manufacturing-use product and the technical grade of each active ingredient in the product is required to support the registration of a manufacturing-use product.

(3) Exemption. No information on the odor of a substance is required if a determination of the odor would involve an inhalation hazard.

(b) Test method. The determination of odor shall be made at room temperature.

(c) Reporting. The odor, if any, should be reported in descriptive terms such as "garlic-like," "characteristic of sulfur-containing compounds," or "characteristic of aromatic compounds."

§ 63-5 Melting point.

(a) When required. If the technical grade of an active ingredient in a product is a solid at room temperature, a determination of the melting point (or melting point range) of each such technical chemical in the product is required by 40 CFR § 158.120 to support the registration of a manufacturing-use product and end-use product. The determination is not required for any substance which sublimes or decomposes.

(b) Test method. The Agency recommends the methods referenced in paragraph (d) of this section.

(c) Reporting. (1) The melting point will be reported in degrees centigrade.

(2) Any decomposition observed in the melting point determination shall be reported along with temperature at which decomposition occurs.

(d) References.

(1) CIPAC MT 2, 45 Fed. Reg. 77341 (Nov. 21, 1980)

(2) OECD Guidelines for Testing Chemicals. May 1981, Section 1, Number 102. Melting Point/Melting Range.

§ 63-6 Boiling point.

(a) When required. If the technical grade of an active ingredient in a product is a liquid at room temperature, a determination of the boiling point range of each such technical chemical in the product is required by 40 CFR § 158.120 to support the registration of both a manufacturing-use product and an end-use product. No data on boiling point are required if the determination would be hazardous.

(b) Test method. The boiling point or boiling point range shall be determined at 760 mm Hg or at a reduced pressure, when appropriate, because of the inherent properties of the chemical.

(c) Reporting. (1) The boiling point or boiling point range shall be reported in °C. The conditions under which the determination was made should be stated.

(2) Any decomposition observed in the boiling point determination shall be reported along with temperature at which decomposition occurs.

(d) References.

(1) OECD Guidelines for Testing Chemicals. May 1981, Section 1, Number 103. Boiling Point/Boiling Range.

§ 64-7 Density, bulk density, or specific gravity.

(a) When required. (1) End-use products. Measurements of the density, bulk density, or specific gravity of the end-use product and of the technical grade of each active ingredient in the product are required by 40 CFR § 158.120 to support the registration of each end-use product.

(2) Manufacturing-use products. Measurements of the density, bulk density, or specific gravity of the manufacturing-use product and of the technical grade of each active ingredient in the product are required to support the registration of each manufacturing-use product.

(3) Limitation. Measurements of density, bulk density, or specific gravity are required only for substances which are in solid or liquid state at room temperature.

(b) Test method. (1) Measurements shall be made at 20°C or 25°C.

(2) When a substance is a solid in particulate form, a measurement of bulk density may be substituted for a measurement of density.

(3) When a substance is a liquid, the specific gravity of the substance shall be determined with reference to water at 20°C.

(c) Reporting. Density and bulk density shall be reported in g/ml.

(d) References. (1) The following references have been published in 45 FR 77338 (Nov. 21, 1980):

(i) CIPAC MT 3.
(ii) ASTM D941-55.
(iii) ASTM D 792-66.
(iv) ASTM D1480-62.
(v) ASTM D1481-62.
(vi) ASTM D1217-54.

(2) OECD Guidelines for Testing Chemicals. May 1981, Section 1, Number 109. Density of Liquids and Solids.

§ 63-8 Solubility.

(a) When required. Data on the solubility of the technical grade of each active ingredient in a product are required by 40 CFR § 158.120 to support the registration of each manufacturing-use product and end-use product.

(b) Test method. The solubility of each substance in distilled water and representative polar and non-polar solvents commonly used for pesticides shall be determined at 20°C or 25°C.

(c) Reporting. Solubility shall be reported in g/100 ml of solvent. If a substance is sparingly soluble, its solubility may be reported in other terms such as ppm (mg/kg).

(d) References.

(1) 40 Fed. Reg. 26879 (June 25, 1975).

(2) 44 Fed. Reg. 16253 (Mar. 16, 1979).

(3) OECD Guidelines, May 1981, May, W.E., S.P. Wasik, and D.H.Freeman. 1978. Determination of the aqueous solubility of polynuclear aromatic hydrocarbons by a coupled column liquid chromatographic technique. Anal. Chem. 50: 175-179.

(4) May, W.E., S.P. Wasik, and D.H. Freeman. 1978. Determination of the solubility behavior of some polycyclic aromatic hydrocarbons in water. Anal. Chem. 50:997-1000.

(5) (Reserved for: OECD Guidelines for Testing Chemical. Section 1, Number 105. Water Solubility.)

§ 63-9 Vapor pressure.

(a) When required. If the boiling point of the pure form of the active ingredient in a product is equal to or greater than 30°C, then a determination of the vapor pressure of the pure form of such active ingredient is required by 40 CFR § 158.120 to support the registration of that product.

(b) Test method. (1) Vapor pressure shall be determined at 25°C.

(2) If the vapor pressure of an active ingredient is less than 1×10^{-7} torr, information demonstrating that the vapor pressure is below that level satisfies the data requirements of this section (unless specifically indicated otherwise by the Agency).

(c) Reporting. The vapor pressure of a substance shall be reported in mm Hg (torr, or other conventional units).

(d) References.

(1) ASTM D3074-72.

(2) 40 Fed. Reg. 26889 (June 25, 1975).

(3) OTS Guidelines; Chem Fate CG 1600, Aug. 1982.

(4) 45 Fed. Reg. 77345 (Nov. 21, 1980).

(5) (OECD Guidelines for Testing Chemicals. Section 1, Number 104. Vapor Pressure Curve.)

§ 63-10 Dissociation constant.

(a) When required. A determination of the dissociation constant for the pure grade of each active ingredient in a product is required by 40 CFR § 158.120 on a case-by-case basis to support the registration of each manufacturing-use product and end-use product.

(b) Test method. The Agency recommends the methods referenced in paragraph (d) of this section.

(c) Reporting. Report the measurement obtained by the methods referenced in paragraph (d) of this section.

(d) References.

(1) OECD Guidelines for Testing Chemicals. May 1981, Section 1, Number 112. Dissociation Constants in Water.

§ 63-11 Octanol/water partition coefficient.

(a) When required. A determination of the octanol/water partition coefficient for the pure grade of each non-polar organic active ingredient in a product is required by 40 CFR 158.120 to support the registration of each manufacturing-use product and end-use product.

(b) Test method. The Agency recommends that the octanol/water partition coefficient be determined using either of the methods specified in paragraph (d) of this section. The determination shall be made at 20°C or 25°C. If the solubility of the test substance is less than 1 ppm, then the concentrations used shall be equivalent to its solubility and to one-half its solubility in water.

(c) Reporting. Report the data and calculations as recommended by any of the methods referenced in paragraph (d) of this section.

(d) References.

(1) OTS Guidelines; CG-1400; August 1982 (2) 45 Fed. Reg. 77350 (Nov. 21, 1980).

(3) [Reserved for: OECD Guidelines for Testing Chemicals. May 1981, Section 1, Number 107. Partition Coefficient (M-Octanol/Water).]

§ 63-12 pH.

(a) When required. (1) End-use products. A determination of the pH of the end-use product and the technical (or purer) grade of each active ingredient in the product is required by 40 CFR § 158.120 to support the registration of each end-use product.

(2) Manufacturing-use product. A determination of the pH of the manufacturing-use product and the technical (or purer) grade of each active ingredient in the product is required to support the registration of each manufacturing-use product.

(3) Limitation. pH determinations are required only for substances which can be diluted or dispersed with water.

(b) Test method. Each substance for which a pH determination is required shall be diluted or dispersed with distilled water. The determination shall be made at 20°C or 25°C in accordance with the method described in paragraph (d) of this section or by any other method of equivalent reliability.

(c) Reporting. Report the measurements obtained by using any of the methods provided in the reference given in paragraph (d) of this section, and in accordance with the test method requirements of paragraph (b) of this section.

(d) Reference.

(1) ASTM E70-74.

(2) OTS Guidelines; CG-1450 August 1982.

§ 63-13 Stability.

(a) When required. Information on the stability of the technical grade of each active ingredient in the product is required by 40 CFR § 158.120 to support the registration of each manufacturing-use product and end-use product.

(b) Test method. The Agency recommends any of the methods referenced in paragraph (d) of this section.

(c) Reporting. The information on stability shall include consideration and discussion of the sensitivity of the active ingredient to metal ions and metal, the stability of the active ingredient at normal and elevated temperatures, and the sensitivity of the active ingredient to sunlight.

(d) References.

(1) CIPAC MT 39.

(2) CIPAC MT 41.

(3) CIPAC MT 46.

(4) CIPAC MT 55.

§ 63-14 Oxidizing or reducing action.

(a) When required. Information on the tendency of a product to act as an oxidizing or reducing agent is required by 40 CFR § 158.120 to support the registration of each manufacturing-use product and end-use product.

(b) Test method. Information on the oxidation or reduction potential of a product may be obtained through a knowledge of the chemistry of the product and by application of the method referred to in paragraph (d) of this section.

(c) Reporting. Report the data on oxidation or reduction action by following the instructions in the method referenced in paragraph (d) of this section.

(d) Reference.

(1) 44 Fed. Reg. 16267 (Mar. 16, 1979).

§ 63-15 Flammability.

(a) When required. A determination of the flash point of a product is required by 40 CFR § 158.120 to support the registration of each manufacturing-use product and end-use product which is a combustible liquid. A flame extension determination for a product is required to support the registration of each end-use product which is an aerosol.

(b) Test methods. (1) The flash point shall be determined by any procedure which is consistent with those listed in paragraph (d) of this section or which is acceptable to any other Federal agency that requires this determination. When the product is intended for packaging under pressure, the flash point is to be determined with the propellent-free portion of the formulation before it is packaged.

(2) The flame extension or flame projection of a product shall be determined by the Standard Method of Test for Flammability of Aerosol Products (ASTM D3065-72).

(c) Reporting. (1) The flash point shall be reported in °F and °C.

(2) The flame extension or flame projection shall be reported to the nearest centimeter or inch.

(d) References.

(1) CIPAC MT 12.

(2) ASTM D56-70.

(3) ASTM D93-73.

(4) ASTM D3278-73.

§ 63-16 Explodability.

(a) When required. Information on the impact explosion characteristics, if any, of a product is required by 40 CFR § 158.120 to support the registration of each manufacturing-use product and end-use product that contains an explosive ingredient.

(b) Test method. The Agency recommends that the impact explodability of a product be determined by a procedure listed in paragraph (d) of this section.

(c) Reporting. Report the data on explodability by following the instructions in the method referenced in paragraph (d) of this section.

(d) Reference. (1) 44 Fed. Reg. 16265 (March 16, 1979).

§ 64-17 Storage stability.

(a) When required. Data concerning the storage stability of a product are required by 40 CFR § 158.120 to support the registration of each manufacturing-use product and end-use product.

(b) Test methods. (1) The test shall be conducted with the product in its commercial package or in smaller packages of the same construction and materials.

(2) The amount of the active ingredient in the product shall be determined at the beginning and at the end of the test period. The applicant shall also determine if any deterioration or degradation products develop in the product during the test period. At the end of the test period, the applicant shall examine the product for physical changes, such as phase separation or "clumping," and, in particular, any changes which would interfere with the usefulness or safe handling of the product if used according to the label directions.

(3) The test period shall be at least one year; and

(4) The test shall be conducted under either of the following conditions:

(i) At 20°C or 25°C, and, if the packaging is permeable, at a relative humidity of 50%; or

(ii) Under warehouse conditions which reflect the expected storage conditions of the commercial product.

(c) Reporting. (1) The report shall describe the duration of the test and the conditions under which the storage stability test was conducted (e.g., temperature, humidity).

(2) The report shall include quantitative analyses for the active ingredient it and on identification and any deterioration or degradation products.

(3) The report shall describe any physical changes in the product during the test period and also the consequences, if any, of such changes for safe handling and use of the product.

(d) Reference.

(1) CIPAC MT 22.

(2) (Reserved for: OECD Guidelines for Testing Chemicals. May 1981, Section 1, Number 114. Viscosity of Liquids.)

§ 63-18 Viscosity.

(a) When required. A determination of the viscosity of a product is required by 40 CFR § 158.120 to support the registration of each manufacturinguse product and end-use product which is a liquid.

(b) Test methods. (1) The Agency recommends that viscosity be determined by any of the methods described in paragraph (d) of this section.

(2) Viscosity shall be determined at 20°C or 25°C.

(c) Reporting. Viscosity shall be reported in terms of poises, stokes, or other conventional units.

(d) References.

(1) CIPAC MT 22

(2) (Reserved for OECD Guidelines for Testing Chemicals. Section 1, Number 114, Viscosity of Liquids,)

§ 63-19 Miscibility.

(a) When required. An evaluation of the miscibility of a product is required by 40 CFR § 158.20 to support the registration of each manufacturing-use product and end-use product which is an emulsifiable liquid, and which also bears directions for dilution with petroleum solvents.

(b) Test method. (1) The evaluation of miscibility shall be made at 20°C or 25°C.

(2) The product shall be mixed with petroleum solvents whose composition reflects those on the label and at the rate specified on the label. After the mixture has stood for 30 minutes, it shall be examined for separation.

(c) Reporting. Report the data on miscibility by following the instructions in the method referenced in paragraph (d) of this section.

(d) Reference.

(1) CIPAC MT 23.

§ 63-20 Corrosion characteristics.

(a) When required. Information on the corrosion characteristics of a product is required by 40 CFR § 158.120 to support the registration of each manufacturing-use product and each end-use product which comes in contact with metal, plastic, or paper containers or closures when commercially packaged.

(b) Combined testing. A study of the corrosion characteristics of a product may be performed in combination with the storage stability test described in § 64-16.

(c) Reporting. Report the data on corrosion characteristics by following the instructions in the method referenced in paragraph (d) of this section.

(d) Reference.

(1) ASTM G31-72.

§ 63-21 Dielectric breakdown voltage.

(a) When required. A measurement of the dielectric breakdown voltage of an end-use product is required by 40 CFR § 158.20 to support the registration of each end-use product which is a non-conductant end-use liquid intended for use in or around electrical equipment.

(b) Test method. The Agency recommends either of the methods referenced in paragraph (d) of this section.

(c) Reporting. Report the data on dielectric breakdown voltage by following the instructions in either of the methods referenced in paragraph (d) of this section.

(d) References.

(1) ASTM D877-67.

(2) ANSI/ASTM D877-76.

Series 64: OTHER PRODUCT CHEMISTRY REQUIREMENTS.

§ 64-1 Submittal of samples.

(a) A sample of the analytical grade of each active ingredient in a product, weighing about 5 grams, and a sample of the technical grade of each active ingredient in a product, weighing about 200 grams, must be submitted (see 40 CFR § 158.120) to support the registration of each manufacturing-use product and those end-use products produced by an integrated formulation system.

(b) When specifically requested by the Agency, the applicant for an end-use product or a manufacturing-use product shall submit samples that are representative of:

(1) The proposed product (about 200 grams) with a composition conforming to the limits certified under § 62-2.

(2) Intentionally-added inert ingredient(s), listed in accordance with § 61-1(b).

(3) A specific product impurity, for which a certified upper composition limit, in accordance with §62-2, may be required.

(4) A specific degradation product or metabolite of either the active ingredient or an intentionally-added inert.

(c) All samples required by this section shall be sent to:

Chief, Chemical and Biological Investigations Branch, Benefits and Field Studies Division, OPP/OPTS, U.S. Environmental Protection Agency, Building 402, ARC-East, Beltsville, Md. 20705